EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

7 April 2022
EMA/212507/2021
European Medicines Agency

[DRAFT] Guidance document on how to approach the protection of personal data and commercially confidential information in documents uploaded and published in the Clinical Trial Information System (CTIS)

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57 # Acronyms

Acronym	Description
Art. 29 WP	The Article 29 Working Party was set up under Article 29 of Directive 95/46/EC. The Art. 29 WP is the independent European working party that dealt with issues relating to the protection of privacy and personal data until 25 May 2018 (entry into application of the GDPR).
ASR	Annual Safety Reporting
CCI	Commercially Confidential Information
CTs	Clinical Trials
CTIS	Clinical Trial Information System
CTR	Clinical Trials Regulation or Regulation (EU) No 536/2014 of the European Parliament and of The Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.
EC	European Commission
EEA	European Economic Area
EMA	European Medicines Agency, also referred to hereafter as the Agency
EU	European Union
EUDPR	Regulation (EU) 2018/1725 of the European Parliament and of the Council of 23 October 2018 on the protection of natural persons with regard to the processing of personal data by the Union institutions, bodies, offices and agencies and on the free movement of such data, and repealing Regulation (EC) No 45/2001 and Decision No 1247/2002/EC (European Data Protection Regulation)
EUPD	European Union Portal and Database
GCP	Good Clinical Practice
GDPR	Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation)
IAM	Identity Access Management
MA	Marketing Authorisation
MAA	Marketing Authorisation Application
MAH	Marketing Authorisation Holder
MSs	Member States
MSC	Member State Concerned
NCAs	National Competent Authorities

Acronym	Description
OMS	Organisation Management Service
RFI	Request for information
RMS	Reporting Member State
XEVMPD	Extended EudraVigilance Medicinal Product Dictionary

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1. General information

1.1. Introduction

Regulation (EU) No 536/2014[1] (hereinafter 'the Clinical Trials Regulation' or 'the Regulation') repeals Directive 2001/20/EC on Clinical Trials[2] and establishes a harmonised approach to the submission, assessment and reporting of clinical trials (CTs) information with the implementation of consistent rules throughout the European Union (EU)/European Economic Area (EEA) Member States (MSs).

The Regulation aims to foster innovation through simplification of the clinical trial application process, and to increase transparency and availability of information on clinical trials and their results.

In accordance with Recitals 66 and 67 and Articles 80 and 81 of the Clinical Trials Regulation, the Agency, in collaboration with the Member States and the European Commission (EC), has the obligation to set up and maintain a EU Portal as a single entry point for the submission of data and documents relating to clinical trials and a EU Database containing the data and documents submitted via the EU Portal in accordance with the Regulation. The EU Clinical Trials Portal and Database are jointly referred to as the EU Portal and Database (EUPD).

The EU Database should contain all relevant information as regards the clinical trials submitted through the EU Portal. To ensure transparency of clinical trials, the EU Database should be publicly accessible and data should be presented in an easily searchable format.

The EUPD is a key instrument to ensure transparency of clinical trial information. The database serves as the source of public information on assessed clinical trial applications, clinical trials conducted from the time of decision, authorisation and finalisation and their results.

The EUPD and associated workspaces provide MSs, the European Commission, the Agency, sponsors and applicants[3] to a marketing authorisation with an effective network to streamline and facilitate the preparation of the flow of information for the authorisation and supervision of clinical trials in the EU.

The EUPD, that enables the submission and storing of clinical trial information, is one of the two components of the Clinical Trial Information System (CTIS).

More specifically, the CTIS encompasses a:

- **Clinical Trial module** consisting of the EUPD, which includes the:
  - Secure domains accessible to Authorities and Sponsors users for the submission of clinical trial applications and trial information during its life cycle, and
  - Public website, which is accessible to the public.
- **Safety module of EudraVigilance (EV)** consisting of the:
  - Repository of Annual Safety Reports (ASRs) in accordance with Article 43 of the CTR for the submission of ASRs in aggregated and anonymised format containing safety information for the investigational medicinal products (IMPs) used during the trial.

[1] Regulation (EU) No 536/2014 of the European Parliament and of The Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.
[2] Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.
[3] Note that where this document refers to 'sponsor users' or 'sponsor domain', this may refer to, respectively as applicable, users acting on behalf of marketing authorisation applicants/holders and related user domain areas in the system.

- The format and content of ASRs is explained in Question 7.33 of Regulation (EU) No 536/2014 Questions & Answers document (in the latest version)[4]

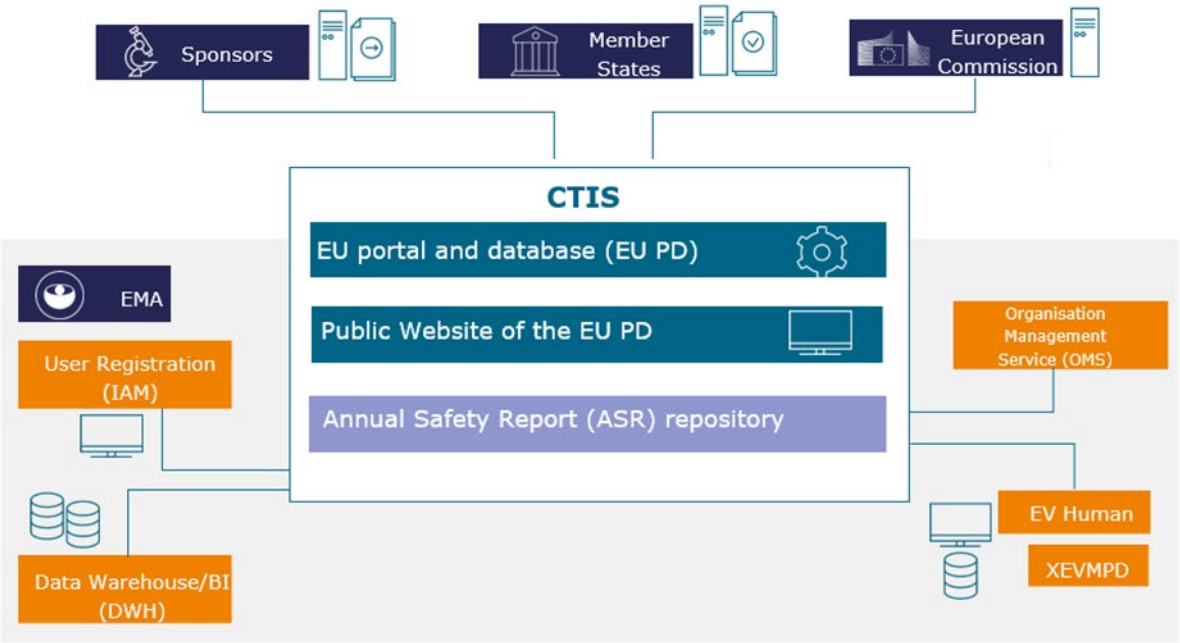
The Clinical Trial Module (EVCTM) for Individual Case Safety Reports (ICSRs) of suspected unexpected serious adverse reactions (SUSARs) related to IMPs is also part of EudraVigilance.

Both, ASRs and ICSRs, are not submitted through the EU Portal to the EU Database and are therefore not subject to publication rules and are not made public.

To streamline the use of the already available information stored in other databases managed by the Agency and to promote consistency and standardisation, CTIS consumes data from the following data sources:

- Extended EudraVigilance Medicinal Product Dictionary (XEVMPD);
- Organisation Management Service (OMS);
- Identity Access Management (IAM).

The interface of CTIS with other EMA data sources is shown in the figure below:



1.2. Scope

This guidance document focuses on the following areas:

- Description of the CTIS structure and components including a description of the functionalities and publication rules for clinical trials information submitted to the CTIS (chapter 2)
- The protection of personal data as part of the clinical trial information submitted to CTIS (chapter 3)
- The protection of commercially confidential information (CCI) as part of the clinical trial information submitted to CTIS (chapter 4)

[4] https://ec.europa.eu/health/system/files/2022-02/regulation5362014_qa_en_1.pdf

- The protection of personal data and CCI in inspection reports (chapter 5)

1.3. Legal framework

The CTR sets out requirements for the protection of personal data, CCI and increased transparency of clinical trials in the EU. These requirements apply to information contained in the EU Database.

Only data and information defined in the CTR being submitted via the EU Portal shall be stored in the EU Database and be subject to the disclosure rules.

Article 81(4) of the Regulation states that the EU Database shall be publicly accessible unless, for all or parts of the data and information contained therein, confidentiality is justified on any of the following grounds:

a) protecting personal data in accordance with Regulation (EU) 2018/1725[5];

b) protecting commercially confidential information, in particular through taking into account the status of the marketing authorisation for the medicinal product, unless there is an overriding public interest in disclosure;

c) protecting confidential communication between Member States in relation to the preparation of the assessment report;

d) ensuring effective supervision of the conduct of a clinical trial by Member States.

Recital 68 of the Regulation sets out what, as a minimum, should be public on each trial (on the basis that it is not in general considered to be confidential): the main characteristics of a clinical trial, the conclusion on Part I of the assessment report for the authorisation of a clinical trial, the decision on the authorisation of a clinical trial, the substantial modification of a clinical trial, and the clinical trial results including reasons for temporary halt and early termination.

No data from the clinical trial application dossier can be made public before the decision on the clinical trial has been taken (Article 81(5) of the Regulation), unless there is an overriding public interest to do so earlier for a particular clinical trial. Accordingly, only applications on which a decision has been made by a Member State concerned (MSC) will be made public. This applies to any decision outcome, on authorisation, authorisation with conditions or whether the authorisation is refused.

Information on applications which are only for assessment of Part I of the dossier (Article 11 applications) will not be made public until a part II has been submitted to the MSC and a decision has been issued by, at least, one of the MSC.

Applications which are not validated or those withdrawn by the applicant before a decision is made will not be made public. In exceptional circumstances, information may be made public if there is an overriding public interest in disclosure.

As outlined above, Article 81 (4) of the CTR refers to the publication aspects of the EU database, taking into account protection of personal data and commercially confidential information.

In addition, the following provisions related to the protection of personal data and CCI should be also taken into account as part of the guidance provided in this document.

- Data protection related provisions

[5] Article 81(4) of Regulation EU (No) 536/2014 refers to Regulation (EU) No 45/2001 replaced by Regulation 2018/1725, the EUDPR

Article 93 of the CTR expressly makes reference to EU data protection legislation i.e., to the now applicable GDPR with reference to the processing of personal data carried out in MSs (including processing by authorities and ethics committees) as well as sponsors, marketing authorisation applicants or holders and the EUDPR which applies to the processing of personal data by the European Commission and the Agency.

Furthermore, the CTR details the need for the protection of personal data as follows:

- Recital 67: *No personal data of data subjects participating in a clinical trial should be recorded in the EU database. The information in the EU database should be public, unless specific reasons require that a piece of information should not be published, in order to protect the right of the individual to private life and the right to the protection of personal data, recognised by Articles 7 and 8 of the Charter (…)*.
- Article 56(1): *All clinical trial information shall be recorded, processed, handled, and stored by the sponsor or investigator, as applicable, in such a way that it can be accurately reported, interpreted and verified while the confidentiality of records and the personal data of the subjects remain protected in accordance with the applicable law on personal data protection.*
- Article 56(2): *Appropriate technical and organisational measures shall be implemented to protect information and personal data processed against unauthorised or unlawful access, disclosure, dissemination, alteration, or destruction or accidental loss, in particular where the processing involves the transmission over a network.*
- Article 81(2): *The EU database shall be established to enable cooperation between the competent authorities of the Member States concerned to the extent that it is necessary for the application of this Regulation and to search for specific clinical trials. It shall also facilitate the communication between sponsors and Member States concerned and enable sponsors to refer to previous submissions of an application for authorisation of a clinical trial or a substantial modification (…).*
- *Article 81(4): The EU database shall be publicly accessible unless, for all or part of the data and information contained therein, confidentiality is justified on any of the following grounds: (a) protecting personal data in accordance with Regulation (EC) No 45/2001;*
- Article 81(6): *The EU database shall contain personal data only insofar as this is necessary for the purposes of paragraph 2.*
- Article 81(7): *No personal data of subjects shall be publicly accessible.*
- Article 93 (1): *Member States shall apply Directive 95/46/EC*[6] *to the processing of personal data carried out in the Member States pursuant to this Regulation.*
- Article 93(2): *Regulation (EC) No 45/200*[7]*1 shall apply to the processing of personal data carried out by the Commission and the Agency pursuant to this Regulation.*

In the context of inspection reports, the CTR sets out the following:

- Article 53(2): *The sponsor shall submit to the Member States concerned, through the EU portal, all inspection reports of third country authorities concerning the clinical trial. When requested by a Member State concerned, the sponsor shall submit a translation of the report or of its summary in an official language of the Union indicated in the request.*

[6] Replaced by Regulation (EU) 2016/679 (GDPR).
[7] Replaced by Regulation (EU) 2018/1725 (EUDPR).

- Article 78(6): *Following an inspection, the Member State under whose responsibility the inspection has been conducted shall draw up an inspection report. That Member State shall make the inspection report available to the inspected entity and the sponsor of the relevant clinical trial and shall submit the inspection report through the EU portal.*

Furthermore, Article 13 of the Commission Implementing Regulation (EU) 2017/556 of 24 March 2017[8] states *(…) The inspection reports submitted through the EU portal shall not contain personal data of clinical trials' subjects.*

- Commercially Confidential Information (CCI) related provisions

Recital 68 clarifies that, for the purposes of the Regulation, in general the data included in a clinical study report should not be considered commercially confidential once the procedure is finalised.

For clinical trials intended to be used in a marketing authorisation application in the EU/EEA, Article 37(4) of the CTR requires that the applicant for a marketing authorisation submits the clinical study report to the EU database within 30 days after the day the marketing authorisation has been granted, the procedure for granting marketing authorisation has been completed, or the applicant has withdrawn the application.

Article 81(4) of the CTR states that "*The EU database shall be publicly accessible unless, for all or part of the data and information contained therein, confidentiality is justified on any of the following grounds: ……..(b) protecting commercially confidential information, in particular through taking into account the status of the marketing authorisation for the medicinal product, unless there is an overriding public interest in disclosure"*

The implementation of the disclosure rules of the Clinical Trial Regulation is without prejudice to the application of Regulation (EC) No 1049/2001[9] and citizens' right to request documents under that Regulation.

1.4. Definitions

For the purposes of the use of the CTIS and this guidance document, the following definitions will apply:

Definition	Description
Aggregated data	Statistical data about several individuals that has been combined to show general trends or values without identifying (either directly or indirectly) individuals within the data.
Anonymisation	The process of rendering personal data anonymous.
Anonymous data (also called as anonymised or irreversibly de-identified data)	Information which does not relate to an identified or identifiable natural person or personal data rendered anonymous in such a manner that the data subject is not, or no longer, identifiable.
Article 29 Data Protection Working Party (Art. 29 WP)	The 'Article 29 Working Party' is the short name of the Article 29 Data Protection Working Party established by Article 29 of Directive 95/46/EC. It provided the European Commission with

[8] COMMISSION IMPLEMENTING REGULATION (EU) 2017/ 556 - of 24 March 2017 - on the detailed arrangements for the good clinical practice inspection procedures pursuant to Regulation (EU) No 536 / 2014 of the European Parliament and of the Council (europa.eu).
[9] REGULATION (EC) No 1049/2001 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 30 May 2001 regarding public access to European Parliament, Council and Commission documents

Definition	Description
	independent advice on data protection matters and helped in the development of a harmonised implementation of data protection rules in the EU Member States. As of 25 May 2018, the Article 29 Working Party ceased to exist, and has been replaced by the European Data Protection Board (EDPB).
Clinical trial information submitted to CTIS	Compilation of data and documents submitted to the CTIS in the context of a clinical trial application, during the evaluation of an application or during the clinical trial life cycle including supervision of the clinical trial and clinical trials results.
Commercially Confidential Information (CCI)	For the purpose of this guidance, any information contained in the clinical trial information submitted to the CTIS which is not in the public domain, or publicly available, and where disclosure may undermine the legitimate economic interest or competitive position of the owner of the information.[10]
Data	Data means characteristics or information, usually numerical, that are collected through observation. The word can also be used to describe statistics (i.e. aggregations or transformations of raw data).
Database	Is an organized collection of data stored as multiple datasets.
Dataset	A dataset is a structured collection of data. A table where each column represents a particular variable and each row corresponds to a different record is an example of a dataset[11].
Data controller (or controller)	'Controller' means the natural or legal person, public authority, agency or other body which, alone or jointly with others, determines the purposes and means of the processing of personal data; where the purposes and means of such processing are determined by Union or Member State law, the controller or the specific criteria for its nomination may be provided for by Union or Member State law. (Article 4(7) of the GDPR, Regulation (EU) 2016/679). or, as applicable to the entity in question 'Controller' means the Union institution or body or the directorate-general or any other organisational entity which, alone or jointly with others, determines the purposes and means of the processing of personal data; where the purposes and means of such processing are determined by a specific Union act, the controller or the specific criteria for its

[10] HMA/EMA recommendations on transparency approved in November 2010 - Recommendations on release of information with regard to new applications for medicinal products before and after opinion or decision on granting of a marketing authorisation (EMA/484118/2010)

[11] See AEPD-EDPS joint paper on 10 misunderstandings related to anonymisation, https://edps.europa.eu/data-protection/our-work/publications/papers/aepd-edps-joint-paper-10-misunderstandings-related_en

Definition	Description
	nomination can be provided for by Union law; (Article 3(8) of the EUDPR, Regulation (EU) 2018/1725).
Data processor (or processor)	Data processor means a natural or legal person, public authority, agency or other body which processes personal data on behalf of the controller Article 4(8) of the GDPR and Article 3(12) of the EUDPR).
Data protection principles	Regulation (EU) 2016/679 and Regulation (EU) 2018/1725 prescribe adherence to 7 data protection principles, i.e.: • Lawfulness, fairness and transparency • Purpose limitation • Data minimisation • Accuracy • Storage limitation • Integrity and confidentiality (security) • Accountability
Data subject	An identified or identifiable natural person to whom personal data relates. An identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person (based on the definition of personal data in Article 4(1) of the GDPR and Article 3(1) of the EUDPR).
Disclosure	The act of making data available to one or more third parties.
EU Clinical Trials Information System (CTIS)	CTIS encompasses the EUPD, the safety module of EudraVigilance for the reporting of Annual Safety Reports (ASR) and interacts with other databases such as IAM (Identity Access Management) and OMS (Organisation Management System) which are also managed by EMA.
EU Clinical Trials Information System (CTIS) user	The natural or legal person(s) or organisation(s) having access to the secure domains of CTIS, that submitted the clinical trial information to the CTIS in the context of a clinical trial application, or that has access to the system during the evaluation of an application, or during the clinical trial life cycle including supervision of the clinical trial.
EU Portal and Database (EUPD)	Regulation (EU) No 536/2014 repealed Directive 2001/20/EC on Clinical Trials and established a harmonised approach to the submission, assessment and reporting of clinical trials (CTs)

Definition	Description
	with the implementation of consistent rules throughout the Member States (MSs). In accordance with Articles 80 and 81 and Recitals 66 and 67 of the Clinical Trials Regulation, the Agency has the obligation, in collaboration with the Member States and the Commission, to set up and maintain both a Clinical Trials Portal, as a single entry point for the submission of data and information relating to clinical trials, and a Clinical Trials Database containing the data and information submitted in accordance with the Regulation.
Joint Controller	Where two or more controllers jointly determine the purposes and means of processing, they shall be joint controllers. They shall in a transparent manner determine their respective responsibilities for compliance with the obligations under this Regulation, in particular as regards the exercising of the rights of the data subject and their respective duties to provide the information referred to in Articles 13 and 14, by means of an arrangement between them unless, and in so far as, the respective responsibilities of the controllers are determined by Union or Member State law to which the controllers are subject. The arrangement may designate a contact point for data subjects. (Article 26(1) of the GDPR) or, as applicable to the entity in question Where two or more controllers or one or more controllers together with one or more controllers other than Union institutions and bodies jointly determine the purposes and means of processing, they shall be joint controllers. They shall in a transparent manner determine their respective responsibilities for compliance with their data protection obligations, in particular as regards the exercising of the rights of the data subject and their respective duties to provide the information referred to in Articles 15 and 16, by means of an arrangement between them unless, and in so far as, the respective responsibilities of the joint controllers are determined by Union or Member State law to which the joint controllers are subject. The arrangement may designate a contact point for data subjects. (Article 28(1) of the EUDPR).
Personal data	'Personal data' means any information relating to an identified or identifiable natural person ('data subject'); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social

Definition	Description
	identity of that natural person. (Article 4(1) of the GDPR and Article 3(1) of the EUDPR).
Special categories of personal data	Personal data revealing racial or ethnic origin, political opinions, religious or philosophical beliefs, or trade union membership, and the processing of genetic data, biometric data for the purpose of uniquely identifying a natural person, data concerning health or data concerning a natural person's sex life or sexual orientation (based on Article 9(1) of the GDPR and Article 10(1) of the EUDPR).
Personal data breach	'Personal data breach' means a breach of security leading to the accidental or unlawful destruction, loss, alteration, unauthorised disclosure of, or access to, personal data transmitted, stored or otherwise processed (Article 4(12) of the GDPR and Article 3(16) of the GDPR).
Process, processes, processing	'Processing' means any operation or set of operations which is performed on personal data or on sets of personal data, whether or not by automated means, such as collection, recording, organisation, structuring, storage, adaptation or alteration, retrieval, consultation, use, disclosure by transmission, dissemination or otherwise making available, alignment or combination, restriction, erasure or destruction; (Article 4(2) of the GDPR and Article 3(3) of the EUDPR).
Pseudonymised, pseudonymisation	'Pseudonymisation' means the processing of personal data in such a manner that the personal data can no longer be attributed to a specific data subject without the use of additional information, provided that such additional information is kept separately and is subject to technical and organisational measures to ensure that the personal data are not attributed to an identified or identifiable natural person (Article 4(5) of the GDPR and Article 3(6) of the EUDPR).
Publishing	The act of making data publicly available.
Redaction	Masking or deletion of data from a document.
Re-identification	The process of analysing data, or combining it with other data, with the result that individuals become identifiable.
Re-identification risk (or re-identification likelihood, risk of re-identification)	The re-identification risk (or likelihood) is the probability in a given dataset of re-identifying an individual, by turning anonymised data back into personal data through the use of data matching or similar techniques.[12]
Study subject, trial participant	For the purpose of Regulation (EU) No 536/2014, a *'subject' is defined as 'an individual who participates in a clinical trial,*

[12] See AEPD-EDPS joint paper on 10 misunderstandings related to anonymisation, https://edps.europa.eu/data-protection/our-work/publications/papers/aepd-edps-joint-paper-10-misunderstandings-related_en.

Definition	Description
	either as a recipient of an investigational medicinal product or as a control'. Article 2(17) of Regulation 536/2014. Use is made in the guidance of the term 'trial participant' as an equivalent to trial 'subject', in order to avoid confusion with the data protection term 'data subject'.
Third Party	Third party means a natural or legal person, public authority, agency or body, other than the data subject, controller, processor and persons who, under the direct authority of the controller, or processor, are authorised to process the data.
Version of the document ***'for publication'***	This is the version of the document provided in the CTIS by the users which should not contain commercial confidential information (CCI) and personal data[13]. It is the responsibility of the user to ensure that this version does not contain such information. See in detail Chapter 2, Section 2.2.1.
Version of the document ***'not for publication'***	This is the version of the document provided in the CTIS by the users which may contain personal data insofar that this is necessary for the purposes listed in Article 81(2) of the Regulation and/or commercial confidential information (CCI). See in detail Chapter 2, Section 2.2.1.

2. Rules of clinical trial information in CTIS pertaining to submission and publication

2.1. Introduction

This chapter describes the type of clinical trial information to be submitted to CTIS and how this should be managed to protect personal data and commercially confidential information (CCI).

The clinical trial information flow starts in the CTIS secure domain with a clinical trial application submitted by the sponsor, or delegated entities, to carry out a clinical trial in the EU/EEA and the corresponding evaluation performed by the EU/EEA Member States concerned.

Following the evaluation of the application, a decision is issued by each Member State concerned for the application, on whether the trial is authorised, authorised with conditions or not authorised. After a decision has been issued by the Member States concerned, the data and documents submitted to the CTIS for the trial will be made available to the public, unless the sponsor has applied for a deferral. Where requested, a deferral will delay the publication of a set of data and documents (e.g. protocol, investigator brochure, informed consent information sheet).

After the authorisation is obtained, the trial can then start, and the Member States concerned can supervise the trial running in their territory. After the initial application, other clinical trial applications can be submitted by the sponsor for the same trial such as substantial modifications to the initial application or the addition of new Member States concerned which are also subject to the assessment and approval from the Member States concerned in question.

[13] With the exceptions defined by the present guidance

In addition to the above, non-substantial modifications to the content of the application dossier can be applied by the sponsor during the trial life cycle up to its completion, as well as notifications to the Member States concerned by the trial, of events of relevance, such as the occurrence of a serious breach or an urgent safety measure. The Member States concerned supervise the conduct of the trial in their territory with different means, including monitoring and assessing safety reports such as Annual Safety Reporting (ASRs), performing Good Clinical Practice (GCP) inspections and having the possibility to apply corrective measures to suspend or revoke trial authorisation, for example.

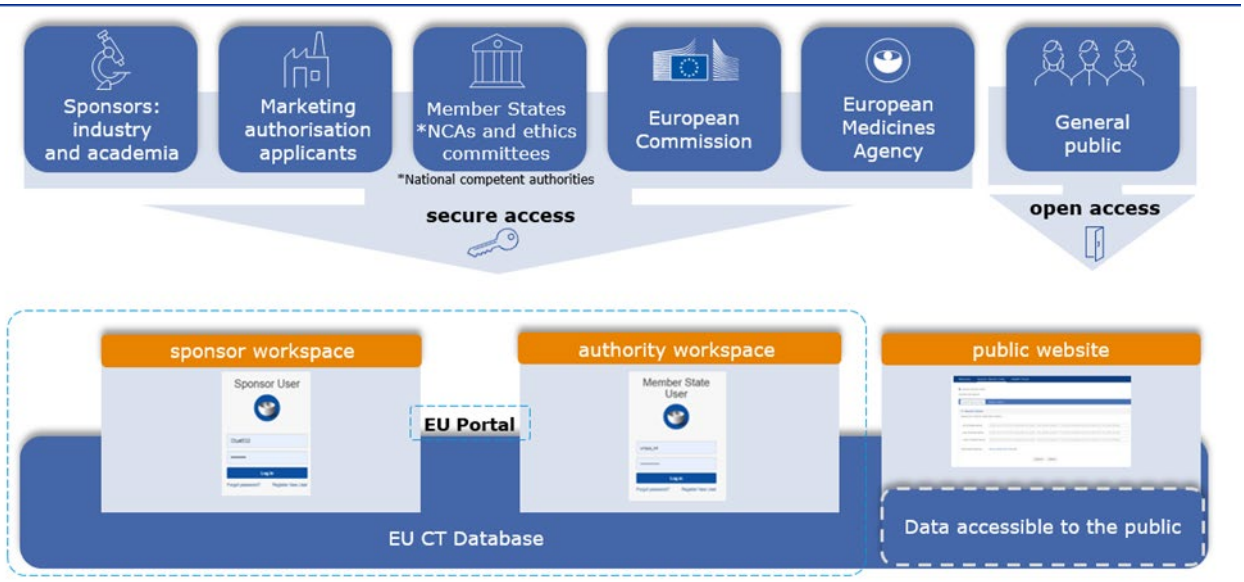
The sequence of events occurring during the trial life cycle might require the collection and processing of personal data for the purposes set out in Article 81(2) of the Clinical Trials Regulation. Data and documents provided by the users in CTIS may also contain information that is considered commercially confidential. As defined in Article 81(4) of the Regulation, personal data of trial participants, as well as other types of personal data, and commercial confidential information are exempted from publication.

Within CTIS secure authority and sponsor domains, the users that can have access to the clinical trial data and documents, for the trials of their concern are: the clinical trial sponsors or delegated parties, EU/EEA Member States (encompassing responsible national competent authorities and Ethics Committees), the European Commission and the Agency.

Access to data and documents in CTIS secure domain is managed through the user profile.

Certain elements of the clinical trial information in CTIS secure domain will also be made available to the general public, via the public website to provide a sufficient level of transparency (Recital 67 and Article 81(4) of the Clinical Trial Regulation).

The image below represents the different domains in CTIS, including sponsors and authorities domains with secure access and a public domain.



2.2. Data and documents uploaded and submitted in CTIS

Data and documents that are provided by the clinical trial sponsors and EU/EEA Member States pertaining to the initial clinical trial application, and later throughout the trial life cycle, include (but are not limited to), the following:

- Cover letter for the clinical trial application;

- Clinical trial protocol[14] and synopsis;
- Medicinal product related documents such as investigator brochure[15], investigation medicinal product dossier, authorisation of manufacturing and import, GMP qualified person certification;
- Details on the Data safety monitoring Board Charter;
- Details on the financial arrangements to conduct the trial;
- Details on co-sponsorship when applicable;
- Part I related request for information (RFI), sponsors responses to the RFI and supporting documentation provided;
- Reporting Member State final assessment report for part I.

Country-specific documents including:

- Proof of Payments;
- Proof of insurance and indemnification;
- Statement of the suitability of the facilities used to conduct the trial;
- Suitability of the principal investigator involved in the trial conduct including Curriculum Vitae and any economic interests and institutional affiliations, that might influence the impartiality;
- Informed consent forms;
- Part II related request for information (RFI), sponsors responses to the RFI and supporting documentation provided;
- Member State concerned final assessment report for part II.

During the trial life cycle:

- Safety related documents provided to monitor the medicinal product benefit/risk ratio, such as Annual Safety reports;
- Documents supporting notifications of early termination[16], temporary halts[17], corrective measures, serious breaches, unexpected events, urgent safety measures, when applicable;
- Inspection reports, when applicable;
- Summary of clinical trial results;
- Full clinical study report[18], when applicable.

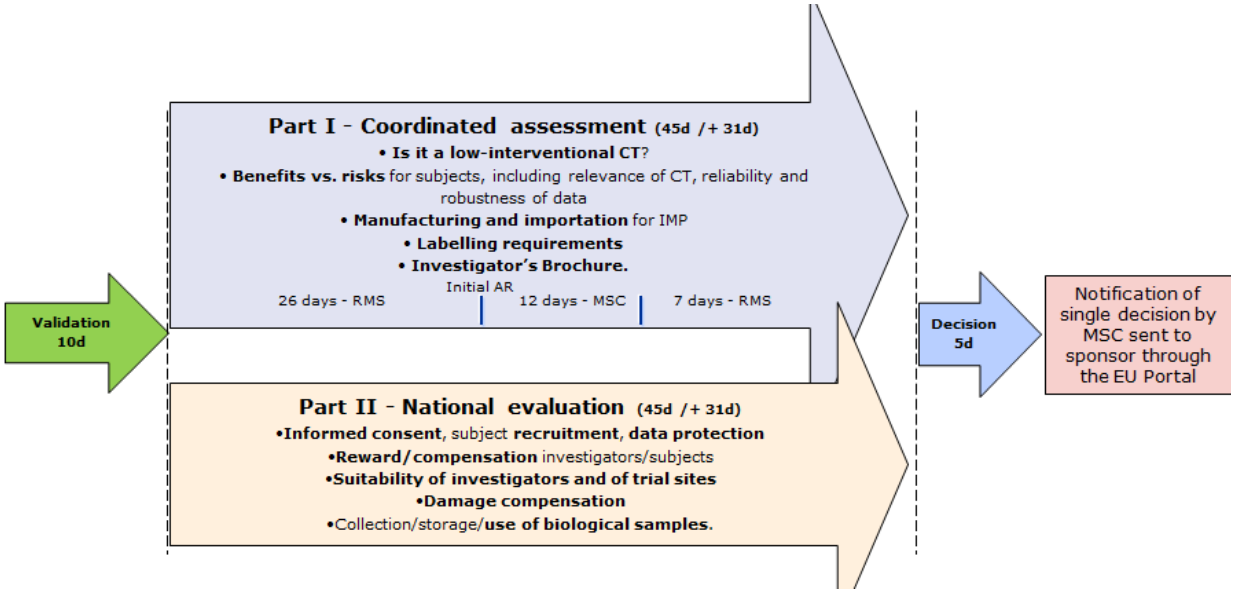
Union Controls plans and reports:

- Union controls plans or programmes for planning purposes

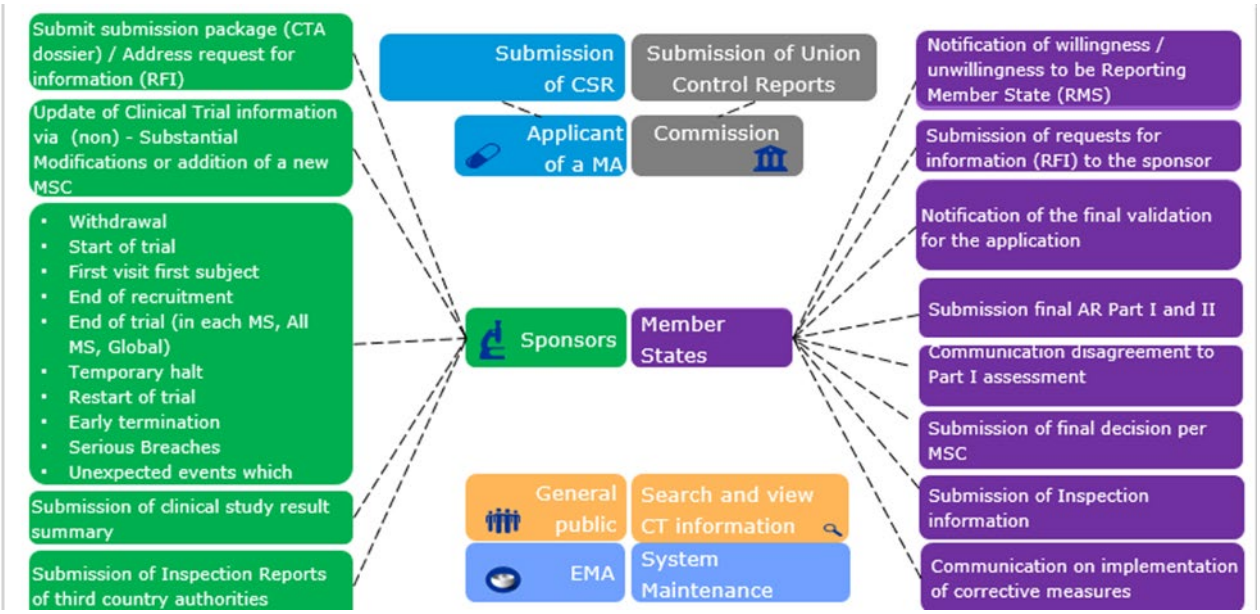
[14] Article 2(22) of Clinical Trials Regulation: 'Protocol' means a document that describes the objectives, design, methodology, statistical considerations and organisation of a clinical trial. The term 'protocol' encompasses successive versions of the protocol and protocol modifications;
[15] Article 2(23) of Clinical Trials Regulation: 'Investigator's brochure' means a compilation of the clinical and non-clinical data on the investigational medicinal product or products which are relevant to the study of the product or products in humans
[16] Early termination of a clinical trial' means the premature end of a clinical trial due to any reason before the conditions specified in the protocol are complied with;
[17] 'Temporary halt of a clinical trial' means an interruption not provided in the protocol of the conduct of a clinical trial by the sponsor with the intention of the sponsor to resume it;
[18] 'Clinical study report' means a report on the clinical trial presented in an easily searchable format, prepared in accordance with Annex I, Part I, Module 5 of Directive 2001/83/EC and accompanying an application for marketing authorisation.

- Union controls reports

A visual representation of the type of data and documents provided for each part of the clinical trial application dossier, including part I and part II, is provided below:



A non-exhaustive list of documents provided by each actor accessing the clinical trial module of CTIS, the EUPD, is presented below. Please consult ***Annex I*** of this document for further details.



2.2.1. Clinical trial information in CTIS and document submissions 'for publication' and 'not for publication'

In CTIS the requirement to provide a document version 'for publication' and 'not for publication' will depend on the document type and content and may not be necessary in every instance.

In instances where both versions are required, for example for GMP documentation with signature of the Qualified person, as applicable, these documents should be provided at the same time.

The following principles apply:

- Sponsors should submit high quality documentation to CTIS to enable an assessment by the Member States concerned. The need to have both versions of documents will depend on the document type and whether protection of personal data and/or CCI would be applicable.
- Only the 'for publication' version of a document will be published with the timing depending on the deferral rules, as applicable.
- For mandatory clinical trial documents submitted to CTIS, in an initial application or during the trial life-cycle, a version 'for publication' must be provided regardless of whether a deferral for publication will be requested for a specific document.
- Personal data if needed during the scientific and regulatory review carried out by the Member States concerned should be provided the document version 'not for publication'. This will enable the Member States Concerned to have all the necessary information for evaluation. Principles of minimisation should be followed however when providing personal data, only as needed in light of Articles 81(6) referring to 81(2) of the regulation.
- Personal data in the document version 'for publication' must be anonymised, for the purpose of public disclosure with exception of personal data of principal investigators at the clinical site, head of the facilities signing the state of compliance of the facility, sponsor legal representative details in line with the requirements of the *Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014"*.
- In general, the data included in a clinical study report should not be considered commercially confidential once a marketing authorisation has been granted, the procedure for granting the marketing authorisation has been completed or the application for a marketing authorisation has been withdrawn.

  In addition, the main characteristics of a clinical trial, the conclusion on Part I of the assessment report for the authorisation of a clinical trial, the decision on the authorisation of a clinical trial, the substantial modification of a clinical trial, and the clinical trial results including reasons for temporary halt and early termination, in general, should not be considered confidential[19].
- CCI can be removed, where applicable. However, all CCI should be available in the document version 'not for publication'. This version should be considered as the original, integral version of the document containing all information required for the assessment by the Member States concerned.
- The CTIS functionality allows for the submission of all required information in the secure domain and provides users access depending on their user profile thus protecting personal data and the legitimate interest of sponsors for what concerns CCI.

More details on what should be protected in the version of the documents 'for publication' in relation to personal data and CCI, can be found in chapter 3 and 4 of this document, respectively.

2.2.2. Use of the deferral mechanism and publication rules

The deferral mechanism in CTIS has been introduced to provide sponsors and Member States with the possibility to delay the publication of clinical trial information with the objective to protect CCI. Publication rules in CTIS are set out in the document Appendix, on disclosure rules, to the of the

[19] Recital 68 of the Clinical Trials Regulation

"Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014", specifically in table 1.

At the time of submission of an initial clinical trial application, clinical trials will be categorised depending on the trial phase and clinical development of the medicinal product(s) being tested.

The following considerations should be taken into account:

- When submitting the initial application, the sponsor has the possibility to choose if they would like to apply for a deferral or not. The extent of the deferral, for the data and documents deferred, and consequent timing for publication of the clinical trial data and documents depends on the selected trial category[20].
- The assessment performed by the RMS/MSC takes into account whether the trial category chosen is correct depending on the trial phase and the clinical development status of the medicinal product(s) being tested. During the evaluation phase, the MSC, in collaboration with and via the RMS, can require sponsors to modify the chosen trial category or the proposed deferral timing (i.e. delay the publication of xx months, yy years) which was documented in the form section of the initial clinical trial application.
- In case of integrated trial phases or adaptive study design, i.e. phase I / II trials, phase II/III trial category should be treated in line with the higher designation[21]
- During the evaluation of an initial application, the RMS can ask the sponsor to apply changes to the deferral settings via a request for information (RFI) on part I. Data and documents provided in the CTA dossier can also be updated if an RFI is raised in that respect. Once a decision is issued on that initial clinical trial application, the timing for publication of the data and documents will be in line with the deferral values selected, if any.
- Regardless if deferrals are selected by the sponsor and endorsed by the RMS/MSC at the time of evaluation of a clinical trial application, the sponsor has the obligation to submit a document version 'for publication' and a version 'not for publication' based on the content of the document and as long as the protection of CCI and personal data is necessary. This rule is also applicable to the documents provided by the Member States Concerned. Note that two versions will not always be needed, it will depend on documents type and content.
- The document version 'for publication' is the one that is published at the designated time, depending if a deferral is applicable for that document. This version should not contain personal data and should not contain information that would still be considered 'commercially confidential' at the time of publication.
- The document version 'not for publication' is the original, integral version containing all the information required by Member State Concerned to perform the assessment. It may contain personal data if necessary in accordance with Article 81(6) referring to the purposes listed in Article 81(2) of the Regulation and it may contain CCI in order to allow for the evaluation of the application carried out by a Member State Concerned.
- Sponsors can modify data and document content while the application (of any type: initial, substantial modification, addition of a MSC) is under evaluation and if an RFI has been raised in that respect. Once that a decision is issued on the application, it will no longer be possible for the

[20] Category 1 trials includes: phase 1 trials, FIH, BE/BA and bio similarity trials. Category 2 includes: phase II and phase III. Category 3 includes: phase IV trials. More details on the Appendix of disclosure rules
[21] Section 4.3.3. paragraph 3 of Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014''

sponsor to modify the data and documents content in that application, even if publication has not yet occurred because of the deferrals authorised.

- Publication of data and documents for the application will occur at the designated time in line with deferrals rule.
- Documents that are not subject to the CTIS publication rules such as quality related documentation and quality assessment reports, financial arrangements, supporting documentation to a sponsor opinion on a corrective measure or a sponsor's reply to an ad hoc request for information raised by the RMS/MSC, are categorised in CTIS as document 'not for publication'.

CTIS functionality to have document version 'for publication' and 'not for publication' depicted below.

- Both document versions 'for publication' and 'not for publication' are to be submitted simultaneously in the CTIS secure domain as part of a clinical trial application, and during the clinical trial life cycle. Substantial modifications can be submitted during the trial life cycle when changes impact on the safety or rights of the subjects or on the reliability and robustness of the data generated in the clinical trial. These substantial modifications are subject to Member States concerned assessment.

  All the applications are subject to publication rules, therefore data and documents of the initial application and the subsequent applications, such as substantial modifications as well as the addition of a new member state concerned and also non substantial modifications will all be available in the public domain. Publication of data and documents for the application will occur at the designated time in line with deferrals rule.

- Sponsors can also submit notifications (e.g. serious breaches, unexpected events, etc..) and summary of results. Also for these documents, in case an update is done, a new version can be submitted. It should be noted that in case there are several document versions 'for publication' due to the updates done, then all the submitted versions of the documents 'for publication' will be available in the public domain.
- The Member States concerned should have sufficient information to carry out their evaluation and supervision of clinical trials at any point in time.
- The published content of sponsor and Member States concerned documents that refer to the same clinical trial/same information should be aligned.
- If a sponsor does not apply for a deferral, the document version 'for publication' will be published at the earliest opportunity, namely: time of the decision. For example, in case of a multinational

initial clinical trial application, the publication will occur as soon as the first MSC issues a decision, i.e. authorise, authorise with conditions, reject the application.

It is strongly encouraged that when a deferral is granted to sponsor, then the same level of confidentiality should also be maintained in the documents produced by the Member States concerned during their evaluation (i.e. assessment reports) and supervision (i.e. inspection reports). Level of protection of CCI in sponsor documents and Member States concerned documents should be similar.

More details on the use of the deferral functionality to protect commercial confidential information can be found in chapter 4 of this guidance document.

Image below summarises for which data and documents deferrals are possible including the maximum timelines.

Actor	Grouping	Category 1 FIH, PK/PD, BE/BA, Bio similarity	Category 2 Phase II and III	Category 3 Phase IV
Sponsor	• Main Characteristics	Publication of final **summary of results**		
Sponsor	• Notifications	Publication of final **summary of results**		
Sponsor	• Subject information sheet	Up to **7 years** after the end of the trial in EU/EEA	Up to **5 years** after the end of the trial in EU/EEA	
Sponsor	• Protocol	Up to **7 years** after the end of the trial in EU/EEA	Up to **5 years** after the end of the trial in EU/EEA	Publication of final **summary of results**
Sponsor	• IMPD S&E sections and Investigator Brochure	Up to **7 years** after the end of the trial in EU/EEA	Up to **5 years** after the end of the trial in EU/EEA	Publication of final **summary of results**
Sponsor	• Responses to RFI	Up to **7 years** after the end of the trial in EU/EEA	Up to **5 years** after the end of the trial in EU/EEA	Publication of final **summary of results**
Sponsor	• Clinical trial results summary for an intermediate data analysis	1. 12 months after interim analysis date 2. up to **30 months** after the end of the trial in the EU/EEA		
Sponsor	• Clinical trial results summary and lay person summary	1. 12 months after the end of trial date in the EU/EEA 2. Up to **30 months** after the end of trial in the EEA		

For category 1 trials that are conducted in paediatric population or are included as part of a paediatric investigational plan (PIP) it is not possible to defer the publication of: main characteristics of the trial, notifications, intermediate data analysis, summary of results and layperson summary

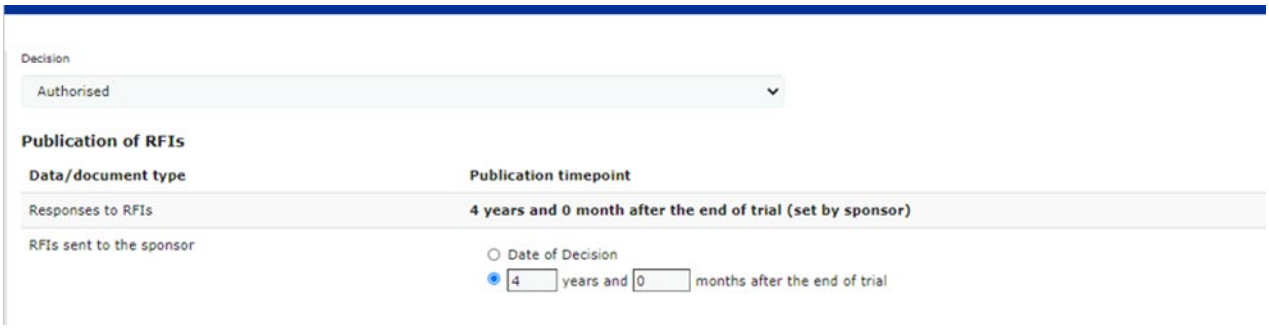
If a sponsor applies for a deferral which is granted by the MSC during the evaluation, then the RMS and MSC can defer the publication of certain documents for the same time period as selected by the sponsor or for a shorter period.

More specifically:

- The **RMS** can defer the publication of information related to **part I**, in relation to request for information (RFI), the final assessment reports and conclusions;
- The **MSC** can defer the publication of information related to **part II**, in relation to request for information (RFI), the final assessment reports and conclusions.

This is defined in the CTIS by each of the Member states concerned at the time of issuing a decision.

The image below provides a CTIS screenshot for illustration purpose.



The following principles apply:

- The publication of the considerations of an RFI sent to the sponsors, and any documents provided with an RFI, can be deferred by the MSC/RMS in line with the deferral timelines requested by the sponsor for their reply to such RFI.
- The publication of MSCs/RMS assessment reports can be deferred in line with the deferral timelines requested by the sponsors for the protocol, investigator's brochure and investigational medicinal product dossier for safety and efficacy (IMPD S&E).
- The deferral of publication of data and documents for a clinical trial will conclude:
  - When the agreed timelines for publication are reached (e.g. 7 years after the end of the trial in the EU/EEA, the submission of summary of results) or
  - If the trial results are used in a marketing authorisation application in the EU and a clinical study report (CSR) has been prepared and submitted to CTIS for the trial. In that instance, the availability of the CSR for a trial will trigger the publication of the deferred data and documents, as applicable.

Further details on the use of the deferral functionality to protect commercial confidential information is provided in chapter 4 of this guidance document.

3. Management of personal data in documents submitted to CTIS

3.1. Introduction

The protection of personal data processed in CTIS is a joint responsibility of the Agency, the European Commission, the Member States (including National Competent Authorities and Ethics Committees) and commercial, non-commercial organisations and academia acting as sponsors of clinical trials and marketing authorisation applicants/holders. This joint responsibility is reflected in the Joint Controllership Arrangement (JCA) for CTIS (europa.eu), which includes in Annex the EMA Data Protection Notice, which is addressed to data subjects and explains the reason for the processing of personal data, the way CTIS collects, handles and ensures protection of all personal data provided, how that information is used and what rights data subjects (e.g., CTIS users, sponsors, investigators, trial participants) have in relation to their personal data.

A clinical trial may be conducted only if it is designed to gather reliable and robust data on an investigational medicinal product[22]. This fundamental principle is confirmed by Article 3(b) of the CTR.

[22] Q1. What are the general obligations of the Clinical Trials Regulation with regard to personal data?

To this extent the sponsor or investigator, as applicable, shall record, process, handle, and store all clinical trial information in such a way that it can be accurately reported, interpreted and verified while the confidentiality of records and the personal data of the subjects remain protected in accordance with the applicable law on personal data protection[23].

Furthermore, the sponsor is required to implement appropriate technical and organisational measures to protect information and personal data processed against unauthorised or unlawful access, disclosure, dissemination, alteration, or destruction or accidental loss, in particular where the processing involves the transmission over a network (Article 56(2) of the CTR) e.g., to the CTIS.

One of these measures to protect personal data include the application of pseudonymisation to safeguard health data of clinical study participants, a special category of personal data according to the GDPR/EUDPR, and, as such, must be strictly protected.

The CTIS has been established to enable cooperation between the competent authorities of the Member States concerned to the extent that it is necessary for the application of the CTR, to facilitate the communication between sponsors and Member States concerned and to enable sponsors to refer to previous submissions of an application for authorisation of a clinical trial or a substantial modification (Article 81(2) of the CTR). Both Member States concerned, and sponsors are responsible for the continuous supervision of the benefit/risk balance of the trial.

To this end, CTIS shall contain personal data only insofar as this is necessary for such purposes (Article 81(6) of the CTR). From a data protection perspective, this meets the principle of purpose limitation and data minimisation i.e., personal data must be adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed[24]

In the context of transparency of clinical trials in CTIS and to protect the right of trial participants to private life and the right to the protection of personal data, Article 81(7) of the CTR sets out that no personal data of subjects shall be publicly accessible, which is further reinforced by Article 81(4) of the CTR that states that the CTIS shall be publicly accessible except where justified to protect the confidentiality of personal data.

To ensure that personal data of data subjects are not made public, these data should be anonymised in the versions of documents 'for publication' (see chapters 3.3) with the exception described in section 3.3.1 and further below.

Chapter 2.1 'Categories of Data Subject and personal data' of the EMA Privacy Statement (Annex II of the CTIS JCA[25]), states the following: *'Should any of these documents contain personal data, as applicable and as required in light of Article 81(2) of Regulation (EU) No 536/2014, this can be provided in the version of the documents 'not for publication'.*

The version of the documents 'for publication' should not contain personal data."

This principle does not apply to information such as the name of the clinical investigator and address of their site, details of the head of the facility declaring the status of compliance and the details of the sponsor legal representative, as this information is required to be in the public domain.

In addition to the EMA data protection notice, ***Annex I*** to this document should be consulted for a more detailed description of the documents submitted via CTIS and the type of personal data that they might typically contain.

[23] Article 56(2) of the CTR
[24] Article 4(c) of the EUDPR and Article 5(c) of the GDPR
[25] Joint Controllership Arrangement (JCA) for CTIS (europa.eu)

The external guidance on the implementation of the European Medicines Agency policy on the publication of clinical data for medicinal products for human use[26] provides direction on the anonymisation of clinical reports and the identification and redaction of commercially confidential information in clinical reports. Key principles are outlined below.

3.2. The principle of anonymisation

Anonymisation refers to information which does not relate to an identified or identifiable natural person or to personal data rendered anonymous in such a manner that the data subject is not or no longer identifiable (Recital 26 of GDPR and Recital 16 of EUDPR). The GDPR/EUDPR does not therefore concern the processing of such anonymous information.

To determine whether a natural person is identifiable, account should be taken of all the means reasonably likely to be used, such as singling out, either by the controller or by another person to identify the natural person directly or indirectly. To ascertain whether means are reasonably likely to be used to identify the natural person, account should be taken of all objective factors, such as the costs of and the amount of time required for identification, taking into consideration the available technology at the time of the processing and technological developments (Recital 26 of GDPR and Recital 16 of EUDPR).

The Article 29 Working Party has issued an Opinion on Anonymisation Techniques[27]. The Opinion discusses that the effectiveness of anonymisation techniques should be checked against three criteria:

i. is it still possible to single out an individual,

ii. is it still possible to link records relating to an individual, and

iii. can information be inferred concerning an individual?[28]

The Opinion also recognises that the use of one individual technique alone cannot meet with certainty the criteria of effective anonymisation. However, some of the criteria may be met in whole or in part by a given technique, therefore a combination of the techniques should be carefully applied together to enhance the robustness of the outcome.[29]

When establishing a process for ensuring an adequate level of anonymisation, the following factors may be considered:

- the likelihood of re-identification being attempted;
- the likelihood the reidentification would be successful;
- the anonymisation techniques which are available to use; and
- the quality of the data after anonymisation has taken place and whether this will meet the needs of the organisation (and the public) using the anonymised information.

For further details, reference should be made to the recommendations of the Article 29 Data Protection Working Party as set out in the Opinion 05/2014 on anonymisation techniques[30] and the external

[26] EMA/90915/2016 Version 1.4
[27] Opinion 05/2014 on Anonymisation Techniques, 0829/14/EN WP216, available: https://ec.europa.eu/justice/article-29/documentation/opinion-recommendation/files/2014/wp216_en.pdf
[28] Ibid, Executive Summary.
[29] Ibid, Section 5.2.
[30] Ibid, Section 5.2.

guidance on the implementation of the European Medicines Agency policy on the publication of clinical data for medicinal products for human use[31].

3.3. General principles on anonymisation of personal data – document version 'for publication'

In the context of CTIS, it is paramount to differentiate between:

a) **Personal data, other than trial participants'**, such as of staff of the sponsor, marketing authorisation applicant/holder, qualified person for GMP documentation, principal investigators etc.. and

b) **Personal data of participants to clinical trials**.

The external guidance on the implementation of the European Medicines Agency policy on the publication of clinical data for medicinal products for human use[32] defines the main principles of anonymisation techniques to protect personal data with particular focus on personal data of trial participants.

Regarding anonymisation of personal data in CTIS the following principles should be considered:

- Anonymisation of documents submitted to CTIS 'for publication' must occur outside of CTIS and be applied consistently across all documents.
- The publication of documents in CTIS can occur at the time of decision on an application, or later in time in case deferrals are applied (see chapter 2).
- Where only one version of a document is provided in CTIS secure domain, namely the version 'for publication' as there is not version uploaded as 'not for publication', this version will be subject to publication and used for review by the MSC(s).
- It is the sole responsibility of the CTIS users, who are uploading the documents, to ensure that the document version 'for publication' are anonymised/redacted in accordance with the applicable process agreed within their organisation. CTIS does not verify if anonymisation/redaction has been applied in version of documents intended for publication.
- When progressing with the submission of the documents via CTIS the authorised user confirms that the recording, storage and publication of the documents in question are in accordance with Union data protection law. A dedicated template will be available for use[33].
- The Agency, as the system administrator, holds the power to delete corrupted, incorrect, or unlawfully processed data, including removing information from the public view[34]. Such requests can be raised by contacting the dedicated EMA service desk: https://servicedesk.ema.europa.eu/. The Agency, or other joint controllers in accordance with the joint controllership arrangement, can also edit the inaccurate or outdated information contained in the CTIS to comply with data protection law.

[31] EMA/90915/2016 Version 1.4
[32] EMA/90915/2016 Version 1.4
[33] Add a link to the template once available
[34] [34] Deletion of incorrect/corrupted documentation should not occur on routine basis but rather on justified grounds to remove corrupted/unlawful information. This should not be seen as an instrument for modification / protection of personal data or commercial confidential information provided by CTIS users that retain the ultimate responsibility.

- It is the sole responsibility of CTIS users to ensure the quality, accuracy and adequacy of anonymisation/redactions applied in structured data or documents uploaded and submitted to CTIS 'for publication'.
- CTIS users authorised to submit data and documents in CTIS, are responsible for ensuring that the submission and anonymisation of documents is done in compliance with the GDPR, EUDPR, any applicable national data protection law, while taking into account relevant guidance and policies issued by the Agency, or by any other responsible authority of Member States or the Union, in relation to CTIS or personal data protection.
- There is a need to apply the right best balance between data utility and achieving an acceptably low risk of re-identification with the objective is to retain a maximum of scientifically useful information for the benefit of the public while achieving adequate anonymisation.
- In this context, the European Commission, Member States, sponsors, sponsor delegated parties, such as clinical research organisations (CROs), marketing authorisation applicants/holders and principal investigators (when acting as sponsors), have joint responsibilities in submitting clinical trial data and documents in accordance with the Clinical Trials Regulation and Union data protection law. They also have joint responsibilities towards the data subjects and should have clear, defined processes in place to deal with any personal data breaches.
- Moreover, sponsors are asked to actively and affirmatively confirm in the form of a statement in their user secure domain, that the processing of personal data in the context, and for the purposes, of CTIS from their side is in full compliance with the GDPR and applicable national data protection legislation.
- Other shared aspects of CTIS falling under the joint controllership scheme, such as the handling of data subjects' rights, is addressed in a published joint controllership arrangement (JCA) for CTIS.

3.3.1. Anonymisation of personal data other than trial participants - documents version 'for publication'

Personal data of staff of sponsors, MAAs, MAHs, qualified persons for GMP documentation, employees of Clinical Research Organisations acting on behalf of the sponsors and Member States experts can be captured in CTIS and related documents in the version 'not for publication' and must be anonymised in the document version 'for publication'.

The following exceptions apply to personal data that should be provided in the document version 'for publication':

- Personal data of principal investigators, legal representative of the sponsors, head of the clinic/institution, which are subject to publication as explained in sections 4.2.2 and 4.2.4 of the Appendix on disclosure rules[35].
- The full name (not signatures) of the sponsor and coordinating investigator signatories of the clinical study report and the identities of the investigator(s) who conducted the trial, which are subject to publication as explained in sections 4.2.5 of the Appendix on disclosure rules[36].

[35] Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014", https://www.ema.europa.eu/en/documents/other/appendix-disclosure-rules-functional-specifications-eu-portal-eu-database-be-audited_en.pdf
[36] Idem.

Where other categories of personal data are required in the document version 'not for publication', they must be anonymised in the corresponding document version 'for publication', except where publication of personal data is necessary in accordance with the rules referenced above.

When applying anonymisation of personal data users can decide to transform or redact the information from the text . For further details, reference should be made to the recommendations of the Article 29 Data Protection Working Party as set out in the Opinion 05/2014 on anonymisation techniques[37] and the external guidance on the implementation of the European Medicines Agency policy on the publication of clinical data for medicinal products for human use.[38]

3.3.2. Anonymisation of personal data of trial participants – documents version 'For publication'

In accordance with Article 81(7) of the Clinical Trials Regulation and prior to being uploaded in CTIS, personal data related to clinical trial participants must be anonymised in the version of documents 'for publication'.

The following elements should be considered when applying anonymisation to the document for publication documents:

Anonymisation techniques [39]

In the context of CTIS, no specific anonymisation methodology is prescribed acknowledging that each anonymisation technique has its own strengths and weaknesses. The robustness of each anonymisation technique is based upon the aforementioned anonymisation criteria and will help in identifying the most suitable technique (or combination of different techniques) to establish an adequate anonymisation process for a given document. Ultimately, the aim is to preserve data utility as much as possible whilst ensuring adequate anonymisation.

The specificities of the relevant data should therefore be taken into consideration when selecting the most appropriate technique(s).

The simplest method of anonymisation is the removal of values for variables which allow direct or indirect identification of an individual from the data. This technique is sometimes called **masking**. Technically, it can be achieved by using a **redaction** tool which ensures that the redacted information is irreversibly blocked out. Masking of pre-specified variables can be done manually and/or may include the use of software that can help identifying pre-specified variables that need redaction. Masking of pre-specified variables is recommended. Removing entire sections of the report where masking is possible is not considered appropriate, and is, therefore, not recommended.

Apart from masking, the main anonymisation techniques are **randomisation and generalisation**[40].

Randomisation is a family of techniques that alters the veracity of the data in order to remove the strong link between the data and the individual. Recommended techniques include **noise addition** and **permutation**. Noise addition can consist of, for example, shifting dates randomly by a few days

[37] Ibid, Section 5.2.
[38] EMA/90915/2016 Version 1.4
[39] The EMA Guidance on the implementation of Policy 0070 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/external-guidance-implementation-european-medicines-agency-policy-publication-clinical-data_en-3.pdf
[40] **Data generalization** is the process of creating a more broad categorization of data in a database, essentially 'zooming out' from the data to create a more general picture of trends or insights it provides

(forward or backwards), based on a uniform, or other type of, distribution. **Permutation**[41] may have limitations as regards clinical utility as relationships between attributes can be destroyed.

The other main family of anonymisation techniques consists of **generalising**, or **diluting** the attributes of the data by modifying the respective scale or order of magnitude. An example would be a trial participant who suffers from asthma, born on 19 August 1978. This date of birth would be generalised to 1978. Recommended generalisation techniques include aggregation and k-anonymity. L-diversity and t-closeness may not be recommended as they limit inferences significantly. Aggregation involves the replacement of a value by a range, e.g. a trial participant's age is replaced with an age range (age of 56 replaced with range of 50 to 60). K-anonymity goes a step further by preventing a trial participant from being singled out since it is grouped with, at least, *k* other trial participants in that range.

Techniques that can be used to anonymise clinical data through mathematical models together with metrics of re-identification are also important. These techniques can be directly applied to the anonymisation of electronic datasets and allow the anonymisation of the copy of the CTIS documents using the underlying clinical data which has already been anonymised.

This may facilitate the anonymisation process and maximise the information included in the copy of the anonymised documents.

The applied anonymisation technique(s) must ensure that the risk of re-identification is acceptably low and in line with requirements for public disclosure. Furthermore, the data transformation resulting from the applied anonymisation techniques must not lead to a different interpretation of the trial documentation.

Clinical trials conducted on rare diseases and/or on small populations may carry a high risk of re-identification of data subjects. Therefore, specific attention should be given to these scenarios. A thorough risk assessment should be performed for such scenarios and the anonymisation of personal data should be adapted to the identified risk. In addition, a quantitative approach to the measurement of the risk of re-identification should be favoured. Such approach is also applicable to genetic information and low frequency events (e.g. rare events, extreme values, unusual treatments, pregnancy outcomes).

3.4. The principle of pseudonymisation – version of documents 'not for publication'

The application of pseudonymisation to personal data can reduce the risks to the data subjects concerned. Pseudonymisation refers to processing of personal data in such a manner that the personal data can no longer be attributed to a specific data subject without the use of additional information, provided that such additional information is kept separately and is subject to technical and organisational measures to ensure that the personal data are not attributed to an identified or identifiable natural person (Article 4(5) of GDPR and Article 3(6) of the EUDPR).

Personal data which have undergone pseudonymisation, which could be attributed to a natural person by the use of additional information should be considered to be information on an identifiable natural person, therefore data protection rules still apply.

The irreversibility of the anonymisation methodologies or techniques is also an important element as it can be used to differentiate from 'pseudonymisation'. Pseudonymisation consists of replacing one

[41] Mathematically a **permutation** counts the number outcomes where the order of what is being counted does matter.

attribute (typically a unique attribute) in a record by another. When pseudonymisation is used alone, the natural person could still to be identified indirectly.

Pseudonymisation reduces the linkability of a dataset with the original identity of a data subject but when used alone will not result in an anonymous dataset. It is, therefore, important to clarify that pseudonymisation is not an anonymisation method but a useful security measure.

Of note for the purpose of the use of CTIS database, pseudonymisation method is applicable only to personal data of trial participants.

3.4.1. Pseudonymisation of personal data of trial participants – documents version ‘’not for publication’

Pseudonymised personal data of trial participants may be contained in CTIS secure domain and if provided they should **only** be included in the document version ‘not for publication’.

A non-exhaustive list of documents that may contain personal data of trial participants is provided below:

- Investigator Brochure
- Paediatric Investigational Plan
- IMPD section S+E
- Unexpected event reports and supporting information
- Urgent safety measure reports and supporting information
- Serious Breach Reports and supporting information
- Clinical study reports
- Assessment reports
- Inspection reports

It should be noted that the principles of data minimisation should be followed when providing pseudonymised personal data of trial participants in the documents ‘not for publication’ in CTIS secure domain. The use of personal data of trial participants should be proportionate. The clinical trial documentation should include sufficient level of details to carry out scientific evaluation and have sufficient data to evaluate the benefit/risk profile of the investigational medicinal product(s) used.

It should be recalled that although personal data of trial participants is presented in a pseudorandomised format, it still qualifies as personal data and should be treated in accordance with the applicable data protection legal requirements.

As stated in Section 3.3.2 and in line with the requirements of Article 81(7), personal data of trial participants must be anonymised by the CTIS users of the secure domain in the version of the documents ‘for publication’ based on the principles described in the sections above. Anonymisation should be done before uploading the documents in CTIS.

4. Guidance on the identification and redaction of commercially confidential information (CCI) in clinical trial

information submitted for publication to the Clinical Trial Information System (CTIS)

4.1. Introduction

The guidance provided in this chapter has been developed as a working tool and a reference document for CTIS users, namely: clinical trial sponsors, marketing authorisation applicants/holders, Member States users, including from National Competent Authorities and Ethics Committees, in order to facilitate the identification of commercially confidential information in clinical trials documentation.

The goals of this chapter are:

- To ensure a common understanding of what may be, or cannot be, considered CCI within clinical trial data and documents provided in an application and during the trial life cycle, and
- To increase consistency in the CCI identified across the various types of information (administrative, quality, non-clinical, clinical)

The Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014'' takes into account the fact that clinical trial data and documents submitted to CTIS may contain information which may constitute commercially confidential information. According to the disclosure rules a number of documents uploaded in the database are not made public, such as the quality-IMPD, assessment reports related to quality aspects, request for information (RFI) and corresponding responses on quality aspects of the application, financial arrangements and more. For a complete list please consult ***Annex I*** to this document.

Equally, certain pieces of information which are present in documents, other than those exempted from publication, may be considered constituting commercially confidential information and therefore may be redacted from the documents to be made publicly available. It is envisaged that as the development plans advance, information which initially was considered confidential may no longer be considered confidential due to the technical and scientific advancements in that research field.

The deferral mechanism described in the disclosure rules and in chapter 2 of this document, can be used by the trial sponsors based on justified grounds and subject to the Member States concerned approval. When the sponsor applies for a deferral, a reasoning should be provided for the proposed timelines to delay the publication of the clinical trial information for which a deferral is proposed by the sponsor.

The deferral rules apply to a subset of the CTA documents such as protocol, investigator brochure, IMPD safety and efficacy, responses to RFI, as well as summary of results[42] (for category I/ phase I trials only) and certain main characteristics[43] (for category I/ phase I trials only).

Once the deferral period elapses, for the applicable documents based on the trial category, the version of the documents 'for publication' uploaded in the CTIS secure domain will be published.

In general, once a marketing authorisation has been granted, the procedure for granting the marketing authorisation has been completed or the application for a marketing authorisation has been withdrawn, information encompassing clinical and non-clinical information is not considered to constitute commercially confidential information. It is acknowledged that in **limited circumstances** administrative, clinical and non-clinical documents may contain CCI, and could, therefore, be subject to

[42] This would not be applicable to clinical trials including paediatric population (i.e. subjects ≤18 years of age) or if the trial is part of paediatric investigation plan.
[43] This would not be applicable to clinical trials including paediatric population (i.e. subjects ≤18 years of age) or if the trial is part of paediatric investigation plan.

redaction prior to publication. In this context it is envisaged that all documents 'for publication' uploaded in the CTIS secure domain can be published subject to redaction of those pieces of information which are, or may still be, considered CCI at the time of the publication.

The redaction of CCI in the CT documentation should therefore be considered by the clinical trial sponsors in conjunction with the available deferral mechanism implemented in CTIS.

It is not envisaged in the use of the system that an extensive redaction of CCI is applied in the version of the documents 'for publication' that will be available in the public domain – in case of deferral - only after few months/years since the end of the trial in the EU/EEA, or at the time of publication of trial results.

In applying redactions in documents for which a deferral is requested/granted, sponsor users should apply a critical thinking when deciding which elements will be considered CCI at the time of publication. It is envisaged that most of the elements considered CCI at the time of the CTA submission, based on the progress of the clinical development, will no longer be considered CCI when the deferral period elapses and therefore will not have to be redacted.

Of note the deferral mechanism is not available in CTIS for clinical study reports (CSRs) submitted by the marketing authorisation applicant/holders[44], and in line with recital 68 of the Regulation[45], CSR content should in principle not be considered CCI at the end of the marketing authorisation process.

4.2. Related policies and guidance documents

While the current guidance applies to documents published on the EU clinical trial database, it is worth raising awareness on how EMA handles CCI in other contexts, namely Policy 0070 and requests for access to documents in accordance with Regulation (EC) No 1049/2001, as the same principles apply. It is therefore recommended to read the present guideline in conjunction with the following policies and guidance documents, some of which were prepared in partnership with NCAs:

- European Medicines Agency policy on publication of clinical data for medicinal products for human use (Policy 0070).
- External guidance on the implementation of the European Medicines Agency policy on the publication of clinical data for medicinal products for human use.[46]
- European Medicines Agency policy on access to documents (related to medicinal products for human and veterinary use)[47] (Policy 0043) – dated 4 October 2018. Policy 0043 should be read in conjunction with the Output of the European Medicines Agency policy on access to documents related to medicinal products for human and veterinary use[48] – dated 4 October 2018.
- HMA/EMEA recommendations on transparency – recommendations on the handling of requests for access to Periodic Safety Update Reports (PSURs)[49] – adopted on 23 November 2009.

[44] In accordance with Article 37(4) of Regulation (EU) No 536/2014, Clinical Study Reports (CSR) are to be submitted to CTIS within 30 days after the day the marketing authorisation has been granted, the procedure for granting the marketing authorisation has been completed, or the applicant for marketing authorisation has withdrawn the application.
[45] For the purposes of this Regulation, in general the data included in a clinical study report should not be considered commercially confidential once a marketing authorisation has been granted, the procedure for granting the marketing authorisation has been completed, the application for marketing authorisation has been withdrawn.
[46] External guidance on the implementation of the European Medicines Agency policy on the publication of clinical data for medicinal products for human use.
[47] European Medicines Agency policy on access to documents (related to medicinal products for human and veterinary use).
[48] Output of the European Medicines Agency policy on access to documents related to medicinal products for human and veterinary use.
[49] HMA/EMEA recommendations on transparency – recommendations on the handling of requests for access to Periodic Safety Update Reports (PSURs).

- HMA/EMA guidance document on the identification of commercially confidential information and personal data within the structure of the marketing authorisation (MA) application – release of information after the granting of a marketing authorisation[50] – adopted on 09 March 2012.
- Principles to be applied for the implementation of the HMA/EMA Guidance on the identification of CCI and PPD in MA Applications[51] – adopted on 09 March 2012.

4.3. Points to consider for identification of commercially confidential information

For the purpose of this guidance, CCI shall mean any information contained in the clinical trial application, or provided during the trial life-cycle, which is not in the public domain or publicly available, and where disclosure may undermine the legitimate economic interest or competitive position of the clinical trial sponsors or marketing authorisation applicants/holders.[52]

When identifying potential CCI, sponsors are strongly encouraged to assess which information in CTIS may not be deferred for any trial category and understand which information and/or documents could be deferred for the study subject to the CTA. For example, in case of a category 2 trial the main characteristics of the trial cannot be deferred, including the pharmaceutical form and strength of the investigational medicinal product(s).

Prior to applying any redactions/protection of CCI, the CTIS users should be aware of the information already available in the public domain concerning their product's development (e.g. study design, development plan timelines and results) and scientific knowledge and advancements within the relevant (for the particular product) therapeutic area(s). Such preparatory work is essential and will reduce the need for unnecessary redactions.

4.3.1. Information that may be considered CCI

It is recommended that where CTIS users, including clinical trial sponsors or marketing authorisation applicants/holders, identify a piece of information such as a word or figure, part of a sentence, part of a paragraph that they wish to include amongst the redactions to protect CCI, they consider whether:

- The piece of information falls under any of the examples of data elements and types of information described in Section 4.5 of this guidance document on 'Information that should not be considered CCI';
- The piece of information meets the definition of CCI.

The extent of the redactions should be limited to the word(s), figure(s), and pieces of text that, in the CTIS user's view, can be considered CCI. The users should not redact entire pages, sub-sections of a document or full tables, especially when, only some sentences within the text or some specific figures within the tables are deemed to be considered CCI.

In order to facilitate the identification of CCI, a short list of specific pieces of information that may carry commercially confidential value is presented below. These examples should not be understood as

[50] HMA/EMA guidance document on the identification of commercially confidential information and personal data within the structure of the marketing authorisation (MA) application – release of information after the granting of a marketing authorisation

[51] Principles to be applied for the implementation of the HMA/EMA Guidance on the identification of CCI and PPD in MA Applications

[52] Working definition of CCI as provided in "HMA/EMA recommendations on transparency approved in November 2010 - Recommendations on release of information with regard to new applications for medicinal products before and after opinion or decision on granting of a marketing authorisation (EMA/484118/2010)". Clinical trial sponsors and marketing authorisation applicants/holders are understood to be the owners of the information submitted in CTIS.

an open and unconditional invitation to redact similar pieces of information present in the clinical trial documentation. In other words, the CTIS user should not consider by default such types of information as being CCI.

The list includes:

- The names of manufacturers or suppliers of the active substance or the excipients, unless disclosure is required as per current pharmaceutical legislation (e.g. for some biological products)
- The excipients quantitative composition of the investigational/authorised product
- Detailed information on the synthesis or manufacture of the active substance,
- Detailed descriptions of the manufacturing and control processes for the investigational/authorised final product
- Information related to future development plans for indications other than the one under investigation and not yet disclosed in the public domain
- New biomarkers or novel methodologies not yet qualified (to the extent that the information is not yet disclosed in the public domain)
- Detailed information concerning innovative analytical methods
- Detailed information on the facilities and equipment available at the sponsors and clinical sites.

4.4. Limiting the need for redactions for CCI

4.4.1. Relevant expertise and consistent decision making process on the identification of CCI

The following elements should be considered when identifying CCI in the clinical trial information submitted to CTIS:

(a) involve in the CCI identification process experts with relevant scientific and technical skills and to (b) follow a consistent decision-making process.

It is envisaged that incorporating these two elements into the CCI identification strategy would not only reduce significantly the need for applying redactions in the CTIS documents, but also increase the efficiency during the process of reviewing the documents in order to identify those pieces of information which may be considered CCI.

The above recommendation aims at reducing the number of instances when the concerns behind the proposed CCI redaction are of high-level nature, unspecific and mainly hypothetical. Moreover the appropriate persons, aware of the actual confidential value of the data, should be involved in the CCI identification process so that the redaction proposals are not based on incorrect assumptions, leading to unnecessary redactions.

In order to avoid such scenarios, CTIS users, especially clinical trial sponsors and marketing authorisation applicants/holders, should follow a consistent decision-making process when evaluating whether a certain piece of information indeed constitutes commercially confidential information or not. According to the definition provided in section 4.3 a piece of information can be considered CCI if it meets simultaneously two criteria: (1) not being available in the public domain or publicly available and (2) it undermines the economic interests or competitive position of the sponsor/marketing authorisation applicants or holders.

Based on this, in order to facilitate the identification of CCI a 3-step approach is proposed below:

First step: rule out the possibility that that particular piece of information is available in the **public domain** (for further guidance please see section 4.5.1). In case the information is available in the public domain, it cannot constitute CCI, no redaction should be implemented and steps 2 and 3 below are not applicable.

Second Step: in case the information is not available in the public domain, it can be determined, in collaboration with experienced professionals having a relevant expertise in the clinical research area, whether the piece of information is **innovative** and whether its release could undermine the economic interests or competitive position of the owner of the information. In this case such information can be considered CCI and be redacted from the documents. If it is determined that the piece of information does not qualify as innovative proceed to step 3.

Third step: In an handful of cases a third step may need to be applied. Despite the fact that the piece of information is not innovative, it is still considered by the sponsor/applicant that its disclosure may undermine the economic interest or competitive position of the owner of the information, then said information can be considered CCI and be redacted from the documents. This step is expected to be employed only in exceptional circumstances.

Once again, it is recommended that, for the above determination, experienced professionals having a relevant expertise in the research area are consulted.

4.4.2. Proactive redaction minimisation approaches

Medical writing can play an important role in reducing the need for redactions. It is expected that embedding a CCI identification and tracing strategy during the writing of the CTIS related documentation would limit the unnecessary dissemination of commercially confidential information in documents where these pieces of information are not essential, required or relevant. Therefore, it is suggested that the sponsors and marketing authorisation applicants/holders consider identifying early during the development plan those pieces of information which are considered CCI, track these as the product evolves and proactively minimise the distribution of these pieces of information across the clinical trial documentation already when the documents are written.

This strategy can be further complemented by employing document templates which specifically indicate which information is required to be included in the documents according to the clinical trial legislation, scientific guidelines and regulatory guidance. As a complementary approach, tagging those pieces of information which are considered CCI at the time the clinical trial documents are written would facilitate the preparation of the document versions meant to be published.

It is envisaged that implementing such approaches would reduce the efforts entailed by preparing separate document versions for publication purposes and it would allow the CTIS users to publish in higher proportion the very same documents which were submitted for scientific evaluation.

4.5. Information that should not be considered CCI

In order to achieve a high level of consistency in the identification of CCI across the clinical trial documents, the sections presented below list some additional examples of types of information which should not be considered CCI[53]. The information pertains to quality, non-clinical and clinical data which, is not considered commercially confidential. Please note that, as described in this document, the

[53] These examples reflect the most common redactions proposed by applicants/MAHs which are usually rejected by EMA in the framework of Access to Documents in accordance with Regulation (EC) No 1049/2001.

list of elements and pieces of information that are not considered CCI is not exhaustive and provides examples only. It is important to note that with an unapproved investigational medicinal product, where development is still continuing towards a future marketing authorization, additional considerations may apply.

4.5.1. Information that is already in the public domain or publicly available

It is recommended that the clinical trial sponsor and marketing authorisation applicants/holders compile a list of the most common websites/locations where information regarding their own medicinal product is usually made available. They may consider creating and maintaining their own specific lists detailing the level of public information concerning their product(s). The following sources of information be included in the list (as a minimum):

- Sponsors, Applicants'/MAHs' own web-site(s).
- EMA web-site (e.g. scientific guidelines, and for, centrally authorised products, the product EPAR,).
- Clinical trials registries (such as CTIS, EU Clinical Trials Register, ClinicalTrials.gov).
- Web-sites of other regulatory authorities within the EU and outside the EU (such as FDA, PMDA, TGA, Health Canada) especially when the product (or another product containing the same active substance) is approved in those specific jurisdictions.
- Scientific literature and articles (such as Textbooks, PubMed, Medline).

The information sources suggested above are not intended to constitute an exhaustive list, but rather to serve as a starting point for the creation of their own (more exhaustive, customized) lists. In this case, the above-mentioned examples should be considered as the minimum number of information sources to be scrutinised in order to reach a basic level of awareness on publicly available information related to the product concerned.

4.5.2. Information that does not bear any innovative features

Information which has already been revealed to certain extent, that can be inferred from information available in the public domain, or has the content of textbooks or scientific guidelines as basis, should not be withhold from the public versions of the clinical trial documents.

The fact that certain pieces of information are not in the public domain as such, (word for word) does not necessarily mean that they should be considered by default to constitute CCI.

In many instances, particular pieces of text contained in clinical trial documents describe how the sponsors and marketing authorisation applicants/holders complied with regulatory and scientific guidelines and how they applied the scientific knowledge available at that time to their own development programme. In essence, these pieces of text do not reveal any novel elements (of any regulatory or scientific nature) as the approaches described in the text are built upon logic and common sense in line with the content of publicly available documents such as:

- Scientific literature and articles (Textbooks, PubMed, Medline).
- Scientific and regulatory guidelines and guidance documents (ICH).
- Treatment/clinical practice/disease management guidelines (Learn societies, HTAs).

4.5.3. Information that would <u>not</u> qualify as commercially confidential

Some data elements should not be redacted from CTIS documentation since they are unlikely to constitute commercially confidential information. Some of these data elements are presented below. The list is not intended to be exhaustive and details of the data elements not considered to be CCI.

The clinical trial documentation contains mainly clinical and administrative related information. However, these CT documents may also contain information of a quality, non-clinical and general or administrative nature, some of which may be considered CCI. Therefore, the elements which are not considered CCI have been grouped into four categories and listed below.

As expected, the list is similar to the one available in Policy 0070 guidance section 3.2.3.

4.5.3.1. General or administrative information

- Unit measurements, in such cases only the actual value may be considered CCI. [e.g.] 2.5mL/kg → [redacted] mL/kg.
- Study identification number(s) (e.g. EudraCT, ClinicalTrials.gov Identifier (NCT…), sponsor's internal study number).
- Names and addresses of investigator sites and the names of the principal investigators at each study site.
- Names of the countries where the clinical study is/was conducted.
- Number (how many) of study sites/research facilities were involved in the research.
- Name of the applicant's/sponsor's own research facility(ies) where clinical studies were conducted (e.g. phase I studies).
- Name of the trial sponsor or the legal entity (CRO) that acted on behalf of the sponsor for clinical trial application submission.
- Names of all CROs and vendors involved in trial-related duties and functions (e.g. central laboratories, IVRS provider, image reading centres).
- Standard Operating Procedure (SOP) numbers and titles.
- Information on worldwide approval status, Marketing Authorisation dates and launch status.

4.5.3.2. Quality-related information

It is recalled that quality related documents are not subject to publication as detailed in the Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014. For example, IMPD-Q will not be made public. However, quality related information may be present in documents, other than IMPD-Q, that are subject to publication.

Therefore, quality related information contained within documents which are subject to publication should be treated according to the principles described above also taking into account the use of deferrals, as applicable . At the time of publication, the following pieces of information should not be considered CCI:

- Structural formula of active metabolite(s) and metabolic pathway(s).

- Lot/batch numbers of the investigational products understood as either test product, active comparator or placebo (excluding manufacturing site(s) IDs that can identify the manufacturing site).
- Excipient names which usually constitute publicly available information detailed in SmPCs and disclosed to investigators and trial participants in the IB and ICF, respectively.
- Function of excipients as such information is widely available in the public domain.
- Excipient batch numbers.
- if a method of measurement is selected from several available methods, the name of the method or the combination of methods and their general description is not CCI.
- High level safety-related information such as a virus inactivation process, ultrafiltration (removal of pyrogen), and the name of a purification process or the operation of a specific material.
- The name of a cell line or strain with genetic recombination, when it is in commercial use or already published (e.g. CHO cell, *E. Coli* K-12).
- Standard storage and shipping conditions of blood or tissue samples such as storage temperature or duration, which are described in related scientific guidelines (e.g. bioanalytical methods).
- Temperature, humidity parameters, and storage duration as applied in stability tests.

4.5.3.3. Non-Clinical-related information

- Information concerning a generally-used/well-known immunohistochemistry method (e.g. ELISA/LC-MS).
- Drug concentration measurements including results.
- The quantification range (lower and upper quantification limits) of pharmacokinetic and pharmacology tests/methods.
- The name and high-level description of test methods should not be redacted where a test is conducted based on a standard dissolution test/method referred to in scientific guidelines.
- Information on radio-labelled molecules including information on the tagging site (unless it constitutes a novelty feature of the method developed by a company, as its disclosure would undermine legitimate economic interest or competitive position).
- Information on scientific advice received from any Regulatory Agency during the development of the product **related to an approved indication** (excluding information for unapproved product or indication). It includes but it is not limited to information on the design and conduct of completed studies for which the results were submitted within a marketing authorisation application, the timing of requesting/obtaining the scientific advice and the names of the Agencies that issued the scientific advice letters.

4.5.3.4. Clinical-related information

- Primary and secondary endpoints (including qualified biomarkers and exploratory endpoints).
- The justification of planned sample size.

- Protocol and protocol amendments (including and not limited to: treatment arms, inclusion/exclusion criteria, allowed concomitant medication(s), reasons for withdrawal and reasons for protocol amendments).
- Statistical methods (including any methods used to analyse the data, imputation methods used for missing data or calculation of the sample size).
- Information on clinical data management (such as query resolution).
- Information audits and inspections carried out during the conduct of clinical trials.
- Literature reviews, meta-analyses and pooled data analyses supporting certain study design elements or certain safety and efficacy claims.
- Bioanalytical methods: name of the methods and the general description together with the validation parameters.
- The fact that approved formulations were changed during the development programme, including the description of any relationships between the different formulations used in the various development programme phases, as well as the timing of such changes and the results of equivalence tests.
- Safety-related information such as adverse reactions (presented in various forms such as individual or aggregated data or within case narratives) regardless of whether they are reflected in the approved product information or whether they were observed in clinical trials or reported before or after authorisation (unless certain elements/adverse reactions are deemed to constitute personal data).
- Plasma drug concentration values and pharmacokinetic and pharmacodynamic parameters.
- General information on PK/PD models, parameters and the results of the PK/PD model simulations.
- Information on scientific advice received from any Regulatory Agency during the development of the product **related to an approved indication** (excluding information for unapproved product or indication). It includes but it is not limited to information on the design and conduct of completed studies for which the results were submitted within a marketing authorisation application, timing of requesting/obtaining the scientific advice and the names of the Agencies that issued the scientific advice letters.

4.6. Balance between deferral rules and redaction of CCI

As mentioned in the introduction section, users should be mindful of the available functionality to request deferral to delay the publication of clinical trials data and documents, see chapter 2 of this guidance document. The deferral mechanism has been introduced to assist clinical trials sponsors and Member States Concerned by reducing the need to apply extensive CCI redactions to their clinical trial information and, instead, delay the publication of such data and documents until a later date when it is expected that only limited information still remains to be considered CCI.

On the other hand, sponsors could avoid the use of the deferral mechanism in case the documents can be published at the time of decision with a **minimal** level of redaction needed.

Sponsors can apply for a deferral at the time of submission of an initial application and the proposed deferral timelines may need to be modified/adjusted following the input received from the MSC/RMS via a request for information (RFI) raised by the RMS, as specified in chapter 2 of the this document.

If a deferral is granted, this has been agreed by all the MSC. Therefore, in case of deferrals, the sponsor should consider prospectively what limited information might still be CCI at the end of the agreed deferral period when the publication will occur. Only details that can still be considered CCI, should be then redacted from the uploaded documents.

The application of redactions to protect CCI should be carefully weighed against the principles of transparency and ease of access to clinical trial information. Redactions applied to a document with deferred publication should take into account that the information contained therein will only become public several years after the end of the trial in the EU/EEA, or the submission of summary of results and, in some cases, after the conclusion of the related marketing authorisation procedure.

In addition, sponsors should consider whether the documents submitted as part of a clinical trial application, for example investigator brochure or IMPD safety and efficacy, are already in the public domain in connection to other trials registered in CTIS public website, or via other public sources, and if any redactions had been applied in these published documents. Consistency should be maintained and the extent of the redactions should be similar across the published documents.

Publication of clinical study reports provided in CTIS by marketing authorisation applicants/holders, cannot be deferred. The Regulation also clearly states that CSR content, in principle, should not be considered CCI. This expectation is confirmed by the experience acquired with the publication of CSRs for centrally approved products as part of Agency's clinical data publication activities (Policy 0070). The Clinical data publication (Policy 0070) annual report confirmed that of 1,308,244 published pages, only 134 contained redactions, which equates to 0.01% of the total published pages.[54] Therefore marketing authorisation applicants/holders are advised that only those elements that, at the time of publication, would be still considered CCI by the party providing the CSR document should be redacted. The extent of redactions in CSR should be kept to the minimum and only when strictly needed to protect CCI.

4.6.1. Deferral and publication of Assessment Reports

In order to align the timing for publication of sponsors documents and Member States Concerned documents, the deferral mechanism has been implemented in CTIS also in the secure authority domain.

Whether by deferral or redaction, or both if applicable, the MSC may ensure that information which is CCI is not in the public domain. Redaction of information to be published must be carried out where CCI is present. When a sponsor has justified a piece of information as CCI, the MSC should take this into account and redact or defer the publication of the information.

When issuing a decision on the authorisation, or not, of an initial application, the Reporting Member State and the Member State Concerned for the trial in question are reminded of the possibility to delay the publication of their corresponding assessment reports and the request for information raised during the assessment.

At the time of decision, the Authority is made aware of the timelines proposed by the sponsors for the deferrals of their clinical trial documentation. If the requested deferral and proposed timelines are agreed, the Authority can defer accordingly the publication of the assessment reports along with the requests for information as follows:

[54] "Clinical data publication (Policy 0070) report Oct 2016- Oct 2017" (EMA/630246/2017).

- The publication of requests for information raised to the sponsor can be delayed for a period of time that is equal to, or shorter than, the period of time selected by the sponsor for the publication of their responses to that particular request for information;
- The publication of assessment reports for part I and part II, and any conditions for the conclusion on part I or II or decision on the trial, can be delayed for a period of time that is equal to, or shorter than, the period of time selected by the sponsor for the publication of the protocol, the IMPD safety and efficacy and the investigator brochure.

The RMS for the trial can defer the publication of the assessment report for part I, while each MSC can defer the publication of the assessment reports for part II.

More details on the deferral timelines can be found in chapter 2 of this guideline, as well as table 1 of the Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014".

It is envisaged that all deferred documents for a clinical trial are published simultaneously regardless of which party uploaded them in CTIS. Therefore, agreement is needed on the timelines for publication of the sponsors and the Member State Concerned data and documents.

In order to reach a consistent level of disclosure of all trial information, users of the authority domain, including those from national competent authorities and ethics committees, should be mindful of the deferral options and the extent of redaction applied by the sponsors in the document versions 'for publication' when preparing and finalising the assessment reports 'for publication' and the extend of redaction that they apply.

5. GCP inspection reports

5.1. Inspection reports provided by EU/EEA regulatory Authorities

CTIS contains a dedicated module to be used and populated by EU/EEA GCP inspectors for the provision of information related to GCP inspections conducted for clinical trials authorised under the regime of the clinical trials Regulation. Provision of such inspection reports to CTIS is in line with the requirements of Article 78 of the Regulation.

In the inspection module of CTIS, the inspectors complete a list of structured data and upload an inspection report for the trials inspected at each single site. GCP inspections can take place in a multitude of different sites including, clinical investigator sites, sponsor offices, various laboratories, and any facility that has been part of the conduct of the trial[55]. Publication rules of the inspection reports in CTIS are based on the following principles:

- Publication of the inspection report(s) will occur when the inspection (of the trials) at all the inspected sites have been completed and the inspection reports finalised;
- In case of inspections done in the context of a marketing authorisation application, inspection report(s) will be published when the Clinical Study Report (CSR) for the inspected trials will be provided in CTIS by the Marketing authorisation applicant[56];

[55] The type of sites where the inspection can take place include, but are not limited to, the following : Analytical and/or clinical facility, clinical investigator sites, sponsor sites (commercial/non-commercial), clinical research organisation (CRO), clinical facility for phase I trials, technical facility, other.
56 This refers to inspections that are conducted as part of an existing marketing authorisation procedure whose number can be provided in the system, for other inspections no further details on future possible inclusion of a trial in a MAA should be provided in CTIS.

- Publication of inspection reports take place via CTIS automated means and based on the implemented system rules. No manual intervention from the inspectors is needed to trigger the publication of the inspection reports. It will occur automatically at the designated time.
- Of note, publication of the inspection reports cannot be deferred while using as such the deferral functionality described in chapter 2 of this document. In case of a legal proceeding the upload of the inspection report in CTIS should be postponed until the completion of the legal case.

Two versions of GCP inspection reports can be uploaded in the CTIS secure authority domain: a version 'For publication' and one 'Not for publication'.

The inspection report of the inspected trials/ facilities should be provided in CTIS, after the consultation steps with the inspectees are completed outside of CTIS system. The inspection reports, containing the final grading of the findings and final GCP inspectors evaluation should be submitted to the CTIS secure domain. These inspection reports should reflect the final outcome of the inspection and not be accompanied by either the initial reports or the responses from the inspectees, where such documentation is available separately as part of the inspection process.

When preparing an inspection report for submission in CTIS the following aspects should be considered by the GCP inspectors:

Protection of personal data: No personal data of sponsor and clinical site staff (except names of principal investigators), interviewed (study) personnel and inspectors writing the report or attending the inspections, should be available in the version of the inspection report 'for publication'.

This entails the names of the persons as well as any direct contact details such as e-mail addresses or phone numbers. The study roles and responsibilities within the trial or company can be disclosed as long as they don't lead to the identification of the individual, or otherwise should not be provided. Of note, if any personal data of study or sponsor personnel would be needed to facilitate collaboration between the parties in light of article 81(2) of the Regulation, such personal data can be included in the version of the documents 'not for publication' which are available only in the CTIS secure domains.

Personal data of principal investigators at the clinical investigator sites will be published via CTIS, so these details do not need to be redacted in the inspection reports uploaded in CTIS, including the version 'for publication'. The same applies to the personal data of sponsor legal representative and head of the facility.

In line with the requirements of Article 13 of the Commission Implementing Regulation (EU) 2017/556, personal data of trial participants must be anonymised.

It is paramount that such information on trial participant details is not publicly disclosed as such and instead anonymised in line with requirements of Article 81(7) of the Regulation.

It follows from the above that due diligence should be applied when inspection reports are drafted and provided to CTIS to ensure that adequate level of protection of personal data is applied.

Commercially confidential information: information already available in the public domain related to the trial(s) subject to inspection, the requested and granted deferrals, as well as the extent of the redactions applied by the sponsors in the uploaded clinical trial documentation, should be considered by the inspectors at the time of the preparation of the inspection reports.

Inspectors can consult the clinical trial data available in the secure domain of CTIS and verify the content of the documents provided by the sponsors, in both versions 'for publication' and 'not for publication' or already published, as applicable.

It should be noted that in case the publication of clinical trial information is deferred, this would imply that, potentially, limited information related to the trial is available in the public domain at the time the inspection report is to be published. In this instance, inspectors should only disclose non-CCI information on the trial and identified findings at the site, in line with the information available in the public domain at the time the report is produced and published.

Inspectors should be mindful of the fact that especially for category I trials, phase 1 trials, First in Human (FIH), and BE/BA trials deferral might apply not only to the trial documents but also to structured data field in CTIS. The applicability of the deferral is clearly visible in the sections 'Form' and 'Evaluation' of a CTA in CTIS. The deferred structured data for category 1 trial, can entail the following types of information: main characteristics of the trial, including for example the trial title, inclusion and exclusion criteria, study endpoints, details on trial design and product related information, including strength and pharmaceutical form.

If deferral is requested and agreed for the publication of details of category 1 trials this should be taken into account at the time of preparation of the inspection report. The same principles apply also to category 2 and 3 trials, for which publication of certain documents can also be deferred, although to a limited extend. Further details are in chapter 2 of this document.

While information of the trial design, medicinal product used, etc.. can be available in the inspection reports version 'not for publication' accessible only to the authorities in the secure domain, due diligence should be applied when producing a version of the inspection report 'for publication'. Any consultation with inspectees or sponsors, as applicable, on the extension of the redaction applied to the inspection reports remains a national decision of the relevant member state inspectorate.

5.2. Inspection reports for inspections carried out by third countries inspectorates provided by the clinical trials sponsors

Sponsors are responsible to provide in CTIS also inspection reports for inspections carried out by third countries authorities of a trial authorised and conducted under the regime of the CT Regulation. This is in line with the sponsors' obligations defined in Article 53 of the CT Regulation. Inspection reports issued by of third countries authorities can be deferred if the trial falls in the category 1 and a deferral has been requested for the notifications[57].

In case of a deferral of an inspection report of third countries authorities, the publication would occur at the time of publication of summary of results. Inspection reports of trials falling under category 2 and 3 are published as soon as they are submitted and their publication cannot be deferred.

The same principles on protection of personal data described in chapter 3 of this document and principles of protection of CCI described chapter 4 of this document also apply to the redaction of third countries inspection reports.

[57] This includes: serious breaches, unexpected events, urgent safety measures, third countries inspectorate inspection reports

Annex 1

Table I [58] – *Data and documents uploaded by the trial sponsor and Marketing Authorisation Applicants/Holders that provide Clinical Study Reports (CSRs), this is not an exhaustive list of all data fields in CTIS but indicative to identify easily data and documents that might contain personal data*

Personal data should be provided in CTIS only when it is required and necessary to facilitate collaboration within the parties [Article 81(6) referring to 81(2) of Regulation 536/2014]

The term 'Clinical Trial Sponsors' in table I and II applies to sponsors or entities working on behalf of the sponsors, like Clinical Research Organisations (CROs)

Data and documents		**Categories of personal data captured in CTIS**	**Categories of data subjects**	**Disclosed**	**Template (if available)**
Data and document category/type	Specific documents (if applicable)				
FORM section					
Cover letter - for the application dossier for initial application and subsequent applications (i.e. SM, additional MSC)		It may include identifying elements e.g. signature	Clinical Trials Sponsors	**Yes**	
Statement of compliance with GDPR		It may include identifying elements e.g. signature	Clinical Trials Sponsors	**Yes**	
Proof of payment *(per MSC)*		It may include identifying elements e.g. signature	Clinical Trials Sponsors	**Yes**	
Modification description *(only for Substantial Modification)*		Not expected	Not expected	**Yes**	
PART I					

[58] This applies to full text documents submitted in an initial clinical trial application, or extract only provided in Substantial Modifications, as applicable

Data and documents		Categories of personal data captured in CTIS	Categories of data subjects	Disclosed	Template (if available)
Data and document category/type	Specific documents (if applicable)				
Clinical trials documents	**Protocol & amendments -** *each version and modification that has occurred*	It may include identifying elements e.g. signature or details of sponsor's staff	Clinical Trials Sponsors	**Yes**	
	Protocol Synopsis	It may include identifying elements e.g. signature or details of sponsor's staff	Clinical Trials Sponsors	**Yes**	
	Data safety monitoring committee charter	It may include identifying elements e.g. full name	Members of the Data safety monitoring Board Charter	**Yes**	
	Justification for low interventional trial	Not expected	Not expected	**Yes**	
	Study design	Not expected	Not expected	**Yes**	
	Summary of scientific advice	It may include identifying elements e.g. full name	It may include identifying elements of employees in the EU regulatory network	**Yes**	
	Scientific advice - quality	Not expected	Not expected	**No**	
	Paediatric Investigational Plan (PIP) opinion	It may include identifying elements of trial participants	Trial participants	**Yes**	

Data and documents		Categories of personal data captured in CTIS	Categories of data subjects	Disclosed	Template (if available)
Data and document category/type	Specific documents (if applicable)				
	Written agreement from the sponsor - *of any previous submitted applications that are associated with this clinical trial*	It may include identifying elements e.g. signature	Clinical Trials Sponsors	**Yes**	
	Sponsor Contact point in the Union	It will include identifying elements	Clinical Trials Sponsors	**No**	Structured data field
	Sponsor Legal representative in the Union	It will include identifying elements	Clinical Trials Sponsors	**Yes**	Structured data field
	Scientific and public sponsor contact point	Expected to be functional	Clinical Trials Sponsors	**Yes**	Structured data field
Medicinal product documents *for test/comparator/auxiliary/ placebo, as applicable*	**Summary of Medicinal Product Characteristics (SMPC)**	Not expected	Not expected	**Yes**	
	Investigator brochure (IB)	It may include identifying elements of trial participants It may include identifying elements e.g. signature	*Trial participants and other personal data*	**Yes**	
	(GMP) Authorisation of manufacturing and import	It may include identifying elements e.g. signature	Manufacturer *TBC*	**Yes**	
	(GMP) Certification by the qualified person (QP) *In the Union that the manufacturing complies with Good Manufacturing Practice (GMP)*	It may include identifying elements e.g. signature	Qualified person (QP)	**Yes**	

Data and documents		Categories of personal data captured in CTIS	Categories of data subjects	Disclosed	Template (if available)
Data and document category/type	Specific documents (if applicable)				
	Quality (IMPD-Q)	Not expected	Not expected	**No**	
	Safety (IMPD-S)	It may include identifying elements of trial participants	Trial participants	**Yes**	
	Efficacy (IMPD-E)	It may include identifying elements of trial participants	*Trial participants*	**Yes**	
	Auxiliary medicinal product dossier (AMPD)	Not expected	Not expected	**No**	
	Placebo medicinal product dossier - quality (IMPD-Q)	Not expected	Not expected	**No**	
	Content of the labelling of the investigational medicinal products	Not expected	Not expected	**Yes**	
PART II					
Recruitment arrangements	**Procedures for inclusion of subjects** - *shall provide a clear indication of what the first act of recruitment is.*	It may include local contact details and names of study personnel	It may include local contact details and names of study personnel	**Yes**	https://ec.europa.eu/health/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-that-will-be-authorised-under-regulation-eu-no-5362014-once-it-becomes-applicable
	Copies of the advertising material - *including any printed*	Not expected	Not expected	**Yes**	

Data and documents		Categories of personal data captured in CTIS	Categories of data subjects	Disclosed	Template (if available)
Data and document category/type	Specific documents (if applicable)				
	materials, and audio or visual recordings				
Subject information, informed consent form and informed consent procedure	**Subject information sheet and informed consent form -** *including each version and modification that has occurred*	It may include local contact details and names of study personnel	It may include local contact details and names of study personnel	**Yes**	https://ec.europa.eu/health/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-that-will-be-authorised-under-regulation-eu-no-5362014-once-it-becomes-applicable
Suitability of the principal investigator	**Principal Investigator Curriculum Vitae (CV)**	Description of the qualification of the principal investigators in a current CV (e.g. basic personal information, contact details, academic background, professional experience etc). Any previous training in the principles of good clinical practice or experience obtained from work with clinical trials and patient care shall be described.	Clinical Trials Principal Investigators	**Yes**	https://ec.europa.eu/health/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-that-will-be-authorised-under-regulation-eu-no-5362014-once-it-becomes-applicable

Data and documents		Categories of personal data captured in CTIS	Categories of data subjects	Disclosed	Template (if available)
Data and document category/type	Specific documents (if applicable)				
		It may include identifying elements e.g. signature			
	Suitability of the investigator other than the investigator's CV	It may include a list of any conditions, such as economic interests and institutional affiliations, that might influence the impartiality of the investigators shall be presented and/or a list of any previous training in the principles of good clinical practice or experience obtained from work with clinical trials and patient care shall be described.	Clinical Trials Principal Investigators	**Yes**	https://ec.europa.eu/health/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-that-will-be-authorised-under-regulation-eu-no-5362014-once-it-becomes-applicable
Suitability of the facilities	**Suitability of the trial site**	It may include identifying elements e.g. signature The written statement issued by the head of the clinic/institution or some responsible person testifying to the suitability of the	Head of the clinic/ institution	**Yes**	https://ec.europa.eu/health/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-that-will-be-authorised-under-regulation-eu-no-5362014-once-it-becomes-applicable

Data and documents		Categories of personal data captured in CTIS	Categories of data subjects	Disclosed	Template (if available)
Data and document category/type	Specific documents (if applicable)				
		facilities and human resources available for the trial is part of the application dossier, will include the name of the person issuing that statement.			
Proof of insurance cover or indemnification		It may contain identifying elements	Clinical Trials Sponsors	**Yes**	https://ec.europa.eu/health/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-that-will-be-authorised-under-regulation-eu-no-5362014-once-it-becomes-applicable
Financial and other arrangements		It may include identifying elements e.g. signature	Clinical Trials Sponsors / Head of the clinic/ institution	**No**	
Compliance with national requirements on data protection		Not expected It may include identifying elements e.g. signature	Not expected Clinical trial sponsor	**Yes**	
Compliance with the use of biological sample		Not expected	Not expected	**Yes**	https://ec.europa.eu/health/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-that-will-be-

Data and documents		Categories of personal data captured in CTIS	Categories of data subjects	Disclosed	Template (if available)
Data and document category/type	Specific documents (if applicable)				
					authorised-under-regulation-eu-no-5362014-once-it-becomes-applicable
Principal investigator (PI) details		It will contain identifying elements of PI	Clinical Trials Principal Investigators	**Yes**	Structured data field
Other documents					
Documents to support responses to the RFI other than quality *(for part I/part II, on any application of the trial (initial authorisation, substantial modifications or addition of a new MSC), as applicable.*	*Any documentation provided by the sponsor to reply to request for information (RFI) raised during the evaluation of an application that do not apply to quality aspects*	It may include identifying elements of trial participants	Trial participants	**Yes**	
Documents to support responses to the RFI on quality or other elements of the dossier not subject to publication *(for any application, as applicable)*	*Any documentation provided by the sponsor to reply to request for information (RFI) raised during the evaluation of an application in relation to quality or other elements of the dossier not subject to publication*	Not expected	Not expected	**No**	
Documents to support responses to sponsor opinion	*Sponsor opinion requested as part of corrective measure*	Not expected	Not expected	**No**	
Documents to support responses to request from *ad hoc* assessment	*Additional information requested by the sponsor as part of an ad hoc assessment*	Not expected	Not expected	**No**	

Data and documents		Categories of personal data captured in CTIS	Categories of data subjects	Disclosed	Template (if available)
Data and document category/type	Specific documents (if applicable)				
Inspection reports of third country authorities - *concerning the clinical trial, including translations of the report or of its summary in an official language of the Union indicated in the request.*		It may include identifying elements e.g. third countries inspectors, sponsor staff or personal data of trial participants	Third countries inspectors, sponsor staff or personal data of trial participants	**Yes**	
Notifications - *of temporary halt, early termination, unexpected events, urgent safety measures, serious breaches*	*Notification supporting documentation*	It may include identifying elements of trial participants	Trial participants	**Yes**	
	Document outlining the follow up measures for clinical trial participants – *in case of a temporarily halt or a premature end of a clinical trial*	It may include identifying elements of trial participants	Trial participants	**Yes**	
Study results	**Summary of results**	It may include identifying elements e.g. signature and personal data of trial participants.	Clinical Trial Sponsors and trial participants	**Yes**	
	Layperson summary of the results	Not expected	Not expected	**Yes**	https://ec.europa.eu/health/system/files/2021-10/glsp_en_0.pdf
	Intermediate data analysis	It may include identifying elements e.g. signature It may include reference to	Clinical Trial Sponsors Trial participants	**Yes**	

Data and documents		Categories of personal data captured in CTIS	Categories of data subjects	Disclosed	Template (if available)
Data and document category/type	Specific documents (if applicable)				
		personal data of trial participants			
	Clinical study report, *i.e. a report on the clinical trial presented in an easily searchable format, prepared in accordance with Annex I, Part I, Module 5 of Directive 2001/83/EC and accompanying an application for marketing authorisation.*	It may include identifying elements e.g. sponsor staff, signature or trial participants details	Clinical Trial Sponsors Trial participants	**Yes**	ICH-E3 STRUCTURE AND CONTENT OF CLINICAL STUDY REPORTS

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1226 **Table 2** – Documents uploaded by the Authorities, including MSC (National Competent Authorities & Ethics Committees) and European Commission

Data and documents		Categories of personal data captured in CTIS	Categories of data subjects	Disclosed	Template (if available)
Data and document category/type	Specific documents (if applicable)				
Draft Assessment Reports for part I and part II		It may include identifying elements of trial participants	Trial participants	**No**	Yes, in CTIS
Final Part I assessment report *For initial and other applications, as applicable*		It may include identifying elements e.g. EU MS assessors It may include reference to personal data of trial participants	EU MS assessors Trial participants	**Yes**	They can be based on the draft AR available in CTIS

Data and documents		Categories of personal data captured in CTIS	Categories of data subjects	Disclosed	Template (if available)
Data and document category/type	Specific documents (if applicable)				
Final Part II assessment report *For initial and other applications, as applicable*		It may include identifying elements e.g. EU MS assessors	EU MS assessors	**Yes**	They can be based on the draft AR available in CTIS
Documents to support requests for information (RFI) to sponsor *for part I/part II, on any application of the trial (initial authorisation, substantial modifications or addition of a new MSC), as applicable.*	*Any documentation provided by the MSC together with request for information (RFI) raised during the evaluation of an application*	It may include identifying elements of trial participants	Trial participants	**Yes**	
Documents to support RFI on quality or other elements of the dossier not subject to publication *(for any application, as applicable)*	*Any documentation provided by the MSC together with request for information (RFI) raised during the evaluation of an application in relation to quality or other elements of the dossier not subject to publication*	Not expected	Not expected	**No**	
Documents to support a request for sponsor opinion in a corrective measure	*Sponsor opinion requested by the MSC as part of corrective measure*	Not expected	Not expected	**No**	
Documents to support a corrective measure	*MSC documents in a corrective measure*	Not expected	Not expected	**Yes**	
Documents to support a request for additional details as part of an ad hoc assessment	*Additional information as part by the MSC as part of an ad hoc assessment*	Not expected *it might include reference to*	Not expected *personal data of trial participants*	**No**	

Data and documents		Categories of personal data captured in CTIS	Categories of data subjects	Disclosed	Template (if available)
Data and document category/type	Specific documents (if applicable)				
		personal data of trial participants			
Inspection report		It may include identifying elements e.g. EU MS inspectors, sponsor staff. It may include reference to personal data of trial participants	EU MS inspectors, sponsor staff. Trial participants	**Yes**	
Assessment reports for serious breaches, urgent safety measures, unexpected events		It may include reference to personal data of trial participants	Trial participants	**Yes**	
Union control plans/programmes/reports		It may include identifying elements e.g. of COM representative or inspected authorities	COM representative or inspected authorities	**Yes**	

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